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PYELITIS, URETERITIS AND CYSTITIS CYSTICA*

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MONTREAL

PYELITIS, ureteritis and cystitis cystica constitute definite pathologic conditions in which cysts are formed in the mucosa or submucosa of the renal pelvis, ureter and bladder respectively.

The first mention of such a condition was made by Morgagni in 1761. Since then it has been described by many pathologists. Litten in 1876 made the first microscopic study. He believed that the cysts resulted from the proliferation of mucous membrane, forming mucosal cysts, or that they were derived from pre-formed glands. Subsequent writers, including Osler, suggested a parasitic origin from coccidial infection. Today the hypothesis advanced by von Limbeck in 1887 and von Brunn in 1893 is generally accepted by most authorities. These authors ascribed the genesis of the cysts to the downward projection, from the inferior layer of the epithelial cells of the mucosa, of epithelial nests, now known as Limbeck–Brunn nests, though more commonly as Brunn's nests. Subsequently, a lumen is developed in the center of the nest by a degenerative or what is more probable a secretory process. At this point the condition may evolve in two directions: first, to the formation of cysts with distended lumina, lined with flattened epithelium, pyelitis, ureteritis or cystitis cystica; second, by a further development of the secretory process, so well described by Stoerk and Zuckerkandl. While the lumen in the epithelial cell nests is still small, the surrounding cells assume a concentric radiating position about it. The inner layer takes on definite characteristics of secreting epithelium, with basally placed nuclei. The inner portion of the cells becomes light, and in it are seen granules which stain with a mucin stain. In other words, the epithelial cells have taken on the characteristics of a secreting epithelium, with the production of true mucin.‡ The resulting condition is known as pyelitis, ureteritis or cystitis glandularis. The cystic and glandular forms are thus very closely related, both resulting from a metaplasia in the epithelium of the urinary tract.

This view of the development of cystitis glandularis has not had universal acceptance. It has been challenged notably by François, who championed the theory that it results from the embryonal inclusion of germinal cells of the lower intestinal tract. This would seem very difficult to combat in the case of the exstrophied bladder, where cystitis cystica and glandularis are found extremely well developed. Their occurrence in the renal pelvis is not so easily explained. The studies of Enderlen and Formiggini, however, would appear to be conclusive. They discovered quite independently that the exstrophied bladders of newborn infants revealed no signs of any cystic or glandular formation. In other words, cystitis cystica and glandularis are postnatal acquisitions.

From a clinical point of view, there is nothing very characteristic of these conditions, apart from a constriction of the ureter, which may follow the ureteral variety. Usually they are quite overshadowed by the underlying condition responsible for the inflammation, of which they are merely a part.

The changes mentioned are not the result of a special form of inflammation but are rather the result of alterations in the bladder epithelium which may develop in the course of any long-continued, not too intense inflammation. While the inciting cause may be found in any kind of chronic irritation, it would appear that the conditions of which we are speaking develop most commonly in the presence of certain special irritating factors. Stone is a frequent concomitant. Inflammatory exudates from infected kidneys may

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‡It should be pointed out that the mucus-like material which is found in the urine of infected bladders is not a true mucin, but a pseudomucin composed of nucleoproteins, derived from degenerating leukocytes.

be the starting point. Mechanical influences alone may bring about the change. For instance, cystic and glandular formations have been found in the bladder in aseptic chronic urinary retention, secondary to prostatic adenoma. When mechanical influences are superadded to infection, they are seen in their most marked development, as in the mucosa of the exstrophied bladder. Chronic cystitis is nearly always present in both cystitis cystica and cystitis glandularis. Where it is not associated, it is presumed to have been present previously, even in intrauterine life.

The condition may develop with extraordinary rapidity. Stoerk and Zuckerkandl report a case of well-marked cystitis cystica and glandularis which developed in forty-two days. While these authors claim that the condition remains during the life of an individual, our own repeated clinical observations show that it may completely disappear. In one case of cystitis cystica, while the underlying infective condition was unchanged, disappearance of bladder cysts was noted, and in a case of cystitis cystica and cystitis glandularis their disappearance followed soon after the removal of the underlying etiologic factors, a ureterocele and a bladder calculus, by cystostomy and temporary bladder drainage.

The experimental work of Giani is most illuminating. In carrying out studies on urinary tuberculosis, Giani introduced capsules containing tubercle bacilli into the bladders of rabbits, by means of a suprapubic cystotomy. The capsules became encrusted and calcified, epithelial nests were formed about them and the typical pathologic picture of cystitis cystica developed. He also produced the condition by curettage of the mucosa. The condition disappeared in three or four months.

In a previous communication, I endeavored to show the relation between leukoplakia and squamous-celled carcinoma, and at a later date Dr. Rhea and I dealt with the relation between cystitis glandularis and mucus-secreting adenocarcinoma of the bladder. In our studies since then we have found the exstrophied bladder a most fertile field of study. Here the two factors of mechanical irritation and inflammation have ample scope, and it is not surprising to discover the two processes of leukoplakia and cystitis cystica or glandularis richly developed side by side. Both conditions, we believe, represent two forms of metaplasia. Both are likely to undergo a further transformation or metamorphosis to carcinoma; squamous-celled in the one case, adeno-carcinoma in the other, the two types of cancer which are found most frequently in the exstrophied bladder, a viscus which is extremely prone to develop malignant changes.

According to Morse, who reviewed the subject in 1928, the literature contains reports of not more than 60 cases of pyelitis cystica, ureteritis cystica or cystitis cystica, mainly of pyelitis cystica and ureteritis cystica. Since that date there have been some additional reports, which, however, do not convince me that the condition is as rare as the paucity of reports would indicate. Certainly cystitis cystica is not a rare condition. Our own experience has shown us that isolated cysts are found not infrequently about the bladder neck, and that even a well-marked development is not unusual. Some years ago, a short study revealed 12 cases in which material obtained at operation or autopsy was available. Morse, in a study of 125 autopsies, practically consecutive, recognized 3 macroscopicallv as pyelitis cystica, ureteritis cystica or cystitis cystica, while cell nests, buds or cysts were found microscopically in 108 cases. During the cystoscopic examination of 190 cases, he found cystitis cystica in 33, or 17 per cent. MacKenzie and Beck in 1936, in 50 autopsies of women subjects, found 16 cases with epithelial nests at the bladder neck and 11 with cysts in the same area.

The finding of a well-marked development of pyelitis cystica and ureteritis cystica is much more unusual. To the 28 cases collected by Morse in 1928, Hinman has added 13, exclusive of the cases based on purely clinical diagnosis, which are dealt with below. Among these are those reported by Urquhart, who, in a series of autopsies in Egypt on patients infected with *Schistosomum haematobium,* found 6 cases of ureteritis cystica. All these cases were discovered at autopsy or operation. To them we shall add 2 cases coming under our own observation but discovered post mortem.

The first is a specimen preserved in the Pathological Museum of McGill University. To Dr. C. B. Keenan of the Royal Victoria Hospital, Montreal, I am indebted for the privilege of reporting it.

A woman of eighty-four was admitted to the hospital with a fracture of the neck of the femur. Suffering from auricular fibrillation during her treatment, she developed two very large decubitus ulcers over her sacrum. She gradually failed, and died two months later. So far as can be learned, there was a history of long-continued urinary infection. Autopsy revealed among other conditions a necrotic cystitis. At one point the bladder had sloughed through into the peritoneal cavity and produced a generalized peritonitis from which the patient died. Pyemic abscesses were found in both kidneys. Both ureters were studded with small thin-walled cysts lined with flattened epithelium (Fig. 1).

The second case is a postmortem specimen for which I am indebted to Dr. D. P. Seecof, late

pathologist of the Jewish General Hospital, Montreal. It was found in a case of calculous pyonephrosis in which a few cysts were discovered in the

FIGURE 1.

Photograph of a postmortem specimen from a case of ureteritis cystica, showing numerous thin-walled cysts in the wall of the ureter.

pelvis and upper ureter. Evidently there had been a long-continued renal infection, associated with the calculi (Fig. 2).

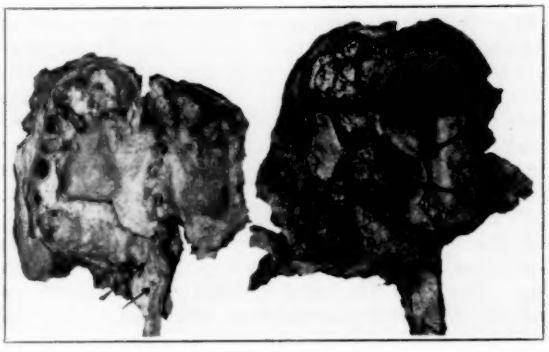

FIGURE 2.

Photograph of a postmortem specimen from a case of calculous pyonephrosis, showing two cysts in the ureter and one cyst in the pelvis.

The main interest in this presentation is with cases in which a clinical diagnosis has been made. Only within the last decade has pyeloureteritis cystica been diagnosed clinically. From the literature I have been able to collect 8 cases, which are here briefly reviewed.

Case 1. Jacoby in 1929 appears to have been the first to make a clinical diagnosis of ureteritis and pyelitis cystica. The patient was a 40-year-old man, who gave a history of chronic urinary infection of 20 years' duration. Renal calculi were present in the left kidney. The bladder showed the typical picture of cystitis cystica. The pyelogram showed a cystic dilatation of the calices and mottled filling defects down the entire left ureter.

Case 2. Joelson in 1929 reported a case in a woman of 44 who entered the hospital because of intermittent hematuria of 13 years' duration. Calculi were present in both kidneys. Cystitis cystica was present. Ureteropyelography revealed dilated pelves and ureters. Small filling defects were noted in the pelves and marked ones in the ureters.

Case 3. Kindall in 1933 confirmed his clinical diagnosis by operation and biopsy. A man of 41 entered the hospital with a right renal colic. He had passed a stone. There were no cysts in the bladder. A clinical diagnosis of pyeloureteritis cystica was confirmed by an exploratory operation. This is the first recorded case in which a clinical diagnosis was confirmed by operation and biopsy. The condition was treated by ureteral dilatation and instillation of 2 per cent silver nitrate solution. Clinical and pyelographic improvement followed.

Case 4. Fite's case (1935) was also confirmed by operation. The patient, a woman of 41, had suffered from urinary frequency for many years, with a recent exacerbation of bladder pain and frequent and painful urination. There was a calculus in the right kidney. The bladder was normal. The ureter showed a moth-eaten appearance. Operation revealed a kidney pyonephrotic in its lower half, which was removed by heminephrectomy. A biopsy from the ureter was secured. The ureter was studded with small, tense, glistening cysts.

Case 5. Chevassu (1936) reported a case of a woman of 51 with a history of pyuria for 26 years. The x-ray film showed a calculus in the right kidney. Ureteropyelograms showed characteristic mottlings. At the operation for the removal of the stone, a section of pelvis was removed for histological study. There were no cysts in the bladder.

Cases 6, 7 and 8. In 1936, Hinman reported 3 cases. The first was a woman of 64, who entered the hospital complaining of severe right lumbar pain of 2 months' duration, with transient attacks of hematuria, and with increased frequency of urination. Pyuria was noted. Cysts were seen in the bladder. Both ureters were dilated. Numerous non-opaque filling defects were observed in both ureters, particularly in their lower two thirds. At the upper ends of both ureters were noted large spherical dilatations, with marked ureteral constrictions immediately beneath. The calices were distended on both sides and there was marked constriction of the caliculopelvic junctures. The pain and bladder symptoms improved after a course of ureteral dilatations and the instillation of a 1 per cent silver nitrate solution. The filling defects in the ureter disappeared, but the intrapelvic changes were unaltered.

His second case was that of a man of 37, who gave a history of pain in the left renal area, with chills, fever, frequency, hematuria, burning and pyuria of 1 year's duration. Three months before admission he had a similar attack. There remained a constant aching pain in the left loin, with frequency, nocturia and burning micturition. Cystoscopy revealed a well-marked cystitis cystica. Both ureters were dilated, and scattered filling defects

were observed in the urograms. The right ureteropelvic juncture was narrowed and there was a slight spherical dilatation of the pelvis or upper end of the ureter above it. The caliculopelvic junctures on both sides were narrowed.

Hinman's third case was that of a woman of 45, who gave a history of burning, frequency and nocturia of 10 years' duration. Her kidney had been removed for hematuria 1 year after the first onset of symptoms. Cystoscopy revealed well-marked cystitis cystica. No filling defects were noted in the ureter. There was narrowing of the caliculopelvic junctures, with dilatation of the calices. There was slight narrowing of the ureteropelvic junctures. In this case he diagnosed a pyelitis cystica, because of the presence of cystitis cystica and the pyelographic change in the pelvis which he believes to be characteristic of a pyelitis cystica.

To these 8 cases we add 2 others in which we have made a clinical diagnosis of pyeloureteritis cystica. Ten cases, therefore, have been diagnosed by urological study, though in 3 only, the cases of Kindall, Fite and Chevassu, was there confirmation by operation and biopsy. In these 3 cases the presence of calculus indicated operative interference.

Case 9. A farmer, a veteran of the World War, was first seen by us in 1926, then aged 29, complaining of urinary frequency and cloudy urine, present since his war

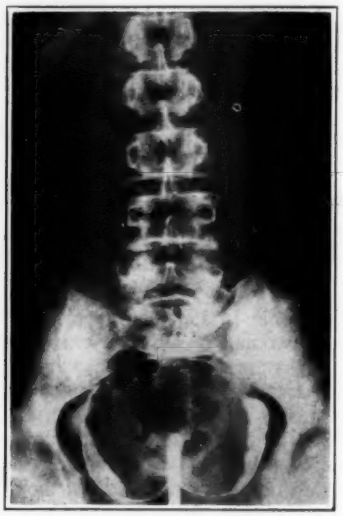

FIGURE 3. *Case 9.*

Ureterogram, in which a clinical diagnosis of ureteritis cystica was made, taken before ureteral dilatation. Note the bilateral ureteral block and the suspicious filling defects in ureters.

service. The frequency was intensified after exposure to cold and fatigue. Occasional pains were felt in the region of the left kidney. At this time urological study was advised, but it was not carried out until 1931, when the patient was admitted to the Montreal General Hospital. There was slight tenderness in both costolumbar areas. The urine contained a moderate quantity of pus. There was frequency every hour by day and two to six times at night. X-ray films showed no calculus. On cystoscopy the bladder orifice was found studded with small translucent cysts, most numerous on the floor and extending backward on the trigone. Both ureteral specimens showed 20 to 30 pus cells per high-power field. Both catheters were blocked by obstructions about 10 cm. up the ureter. X-ray studies with sodium iodide revealed dilated ureters below the point of obstruction (Fig. 3). No filling defects were seen.

It was not possible to do anything more for the patient at this time owing to his unwillingness to follow any treatment. He was in the hospital on several occasions in 1936 and 1937 for brief examinations. On these occa-

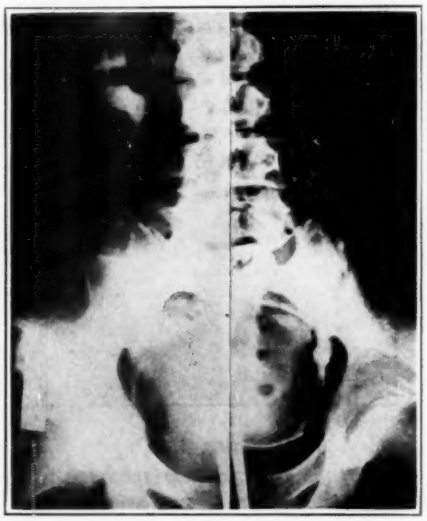

FIGURE 4. *Case 9.*

Composite urogram taken after ureteral dilatation. Note the filling defects in the left lower and right upper ureters.

sions single attempts at ureteral dilatation were made, with some improvement, as on the patient's last visit in August, 1937, he stated that his frequency was better than it had been for many years. He suffered, however, from low back pain and fatigue on exertion, and the urine still contained pus. Urine culture revealed no bacterial growth. At cystoscopy, cysts were always found on the trigone and around the bladder neck. The lower ureters were still tortuous and dilated. Only in August, 1937, were we able to demonstrate any filling in a kidney, and that was the right one. Intravenous pyelograms were most unsatisfactory because of the poor visualization. The combined renal function was definitely impaired. The urea concentration factor on August 14, 1937, was only 33.

The cystoscopic report of August 14, 1937, reads as follows: "The internal orifice and trigone are covered with cysts. Several cysts are noted close to the ureteral orifices." Both kidney specimens contained pus. Pyelography on this occasion revealed the following: "The tip of the catheter on the right side has reached a level between the 4th and 5th lumbar vertebrae. On the left side the catheter has reached the level of the upper border of the left ischial spine. The pelvis and calices of the right kidney are filled. No injection on the left. There is slight dilatation of the pelvis of the right kidney, with rather irregular blunting of the upper calyx. Both ureters are tortuous and dilated. On the left ureter, in its lower

third, are seen several longitudinal filling defects, which are suggestive of a ureteritis cystica." (Fig. 4.)

In this case, in view of the long history of chronic urinary infection, the presence of cystitis cystica, the dilated and strictured ureters and the filling defects in the left ureter, we have made a clinical diagnosis of ureteritis cystica, with a suspicion of pyelitis cystica. Ureteral dilatation, or the little we have been able to perform, seems to have been followed by some improvement.

Case 10. A man of 71 was admitted to the medical service of the Montreal General Hospital in June, 1937, complaining among other things of a nocturia of 3 years' duration. He had a chronic bronchitis and hypertensive cardiovascular disease. For the previous 3 years he had had frequency, by day every 2 hours, by night three to four times. In the 3 weeks previous to admission the symptoms had been greatly aggravated. He passed small quantities of urine every 30 minutes, and complained of burning and dribbling. For several days he had been unable to sleep on account of persistent suprapubic and groin pain. His prostate was moderately enlarged. The urine contained a moderate quantity of pus, 1 to 5 cells per high-power field. The frequency subsided somewhat after resting in bed.

As the routine x-ray films showed a shadow in the left kidney region, suggesting a calculus, the patient was seen by the Urological Service on June 10.

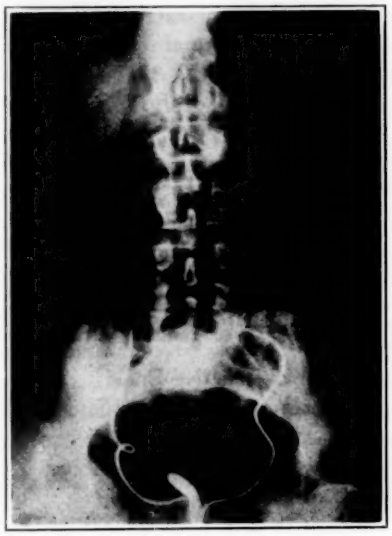

FIGURE 5. *Case 10.*
X-ray film showing a calculus in the left kidney.

Cystoscopy showed a slight prostatic enlargement. The ureters were catheterized, the right easily, the left with difficulty and only partially. No pus was found in the ureteral specimens. Pyelography showed the opaque shadow to be situated in the inferior calyx of the left kidney (Fig. 5). This pelvis was incompletely filled. Multiple circular filling defects were observed on both ureters and the right kidney pelvis.

Four days later, the patient was again cystoscoped. On this occasion, a more careful search of the bladder revealed the presence of two cysts at the bladder neck. Garceau catheters were passed up both ureters for 5 cm. Culture of the right kidney urine showed *Staphylococcus aureus.* That of the left side gave no growth. Pyelograms showed clearly the presence of the filling defects in the left ureter and left pelvis (Fig. 6).

The patient had a definite renal insufficiency, his urea concentration factor being only 22. On account of this, his age and his hypertensive cardiovascular condition, operation for the removal of the calculus was neither desired nor urged. Similarly, further ureteral dilatations were not possible.

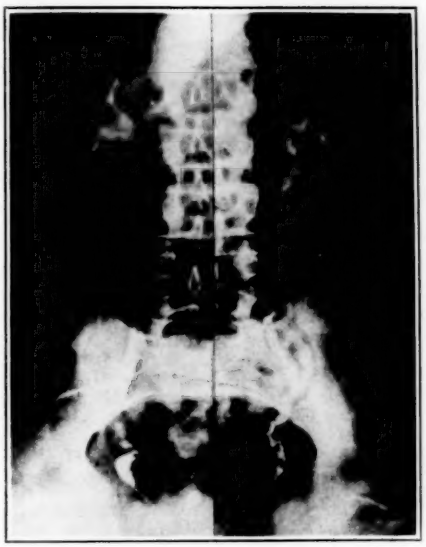

FIGURE 6. *Case 10.*
Composite urogram. Note the filling defects in both ureters and kidney pelves.

While operative confirmation was not secured, it is believed that this is a definite case of pyeloureterocystitis cystica.

SYMPTOMS

There are no symptoms pathognomonic of the condition, since they are found in patients suffering usually from long-standing urinary tract infections, and the symptoms are identical with those of such an infection or conditions such as calculus, so often associated. From this fact it happens that the condition is usually found in older individuals. That age is not an essential requisite is seen in the fact that the exstrophic bladder shows the condition in its most marked development. It occurs about equally in both sexes, though one would expect from the more numerous obstructive factors present in men that they would be more likely to suffer from it. Calculus is frequently found. Five of the 10 clinical cases of pyeloureteritis cystica had renal stone. Occasionally copious hematurias are reported. This symptom has not infrequently been responsible for a diagnosis of tumor. Only at the nephrectomy was the true condition revealed. There is a very definite tendency to bilaterality. The bacteriological flora is very variable, including *Staphylococcus*

aureus, streptococcus, *Bacillus coli* and *Bacillus pyocyaneus.*

DIAGNOSIS

The presence of cysts above the surface of the bladder in the region of the bladder neck makes recognition of cystitis cystica by cystoscopic observation fairly easy (Figs. 7 and 8). Cystitis

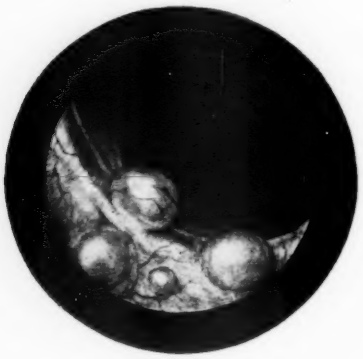

FIGURE 7.

Cystoscopic appearance of the bladder in a case of bilateral nephrolithiasis, with cystitis cystica and suspected ureteritis cystica.

glandularis presents an irregular or mammillated appearance difficult to distinguish from cystitis cystica, except in microscopic sections. At other times,

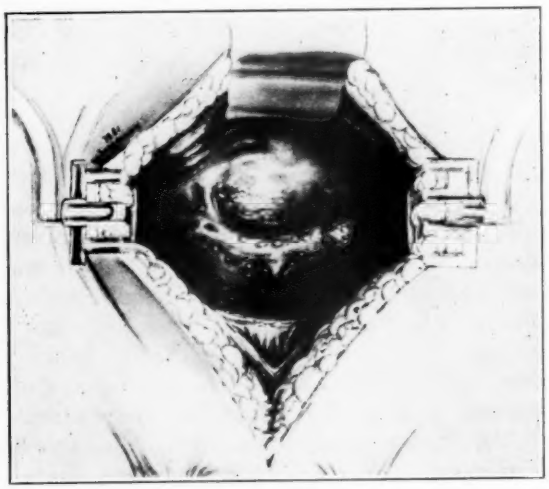

FIGURE 8.

Photograph of a drawing made at operation in a case of cystitis cystica and cystitis glandularis. There were numerous cysts on the bladder base. The patient had a vesical calculus and a ureterocele. Complete cure followed operation.

cystitis glandularis may present itself as an ulceration, red and bleeding, or may be covered with a necrotic membrane. One of our most characteristic sections was secured at autopsy. No gross lesion was observed. The condition was not suspected until routine microscopic sections taken from the bladder neck revealed typical cystic and glandular cystitis, with associated leukoplakia.

The diagnosis of pyelitis and ureteritis cystica is not so simple, but it should be obvious that with our present methods of urological study they may be readily recognized. Wherever cystitis cystica is noted, the upper urinary tract should be given a more than usually close scrutiny. Cystitis cystica is usually associated with a pyelitis or ureteritis cystica, or both, though not always. In our second case it was only after noting the ureterographic picture that a careful search of the bladder revealed the presence of a few cysts in that viscus.

Of prime importance in diagnosing ureteritis or pyelitis cystica, is the occurrence of vacuoles, bubbles or non-opaque filling defects in the urogram. Before their true significance was realized, they were frequently confused with air bubbles or papillomas. Another finding of significance is a dilatation, tortuosity or constriction of the ureters. In the pelvis, there is found a spherical calicular dilatation, with narrowing of the caliculopelvic junctures. Hinman is insistent on the value of this sign, as also on the narrowing at the ureteropelvic juncture, with a spherical dilatation above. One must confess that such a finding in the absence of the typical vacuoles of filling defects is not entirely inconsistent with a diagnosis of chronic pyelonephritis.

TREATMENT

This should very naturally be directed to the underlying inflammatory process. Search for a causative factor should be our first objective. If this factor is an obstructive one its removal where possible may bring about a complete subsidence of symptoms, and, as our own experience has taught us, particularly in the bladder variety, a complete disappearance of the cysts.

Such therapy is easier to achieve in cystitis cystica, where the obstructing condition may be easily recognized and dealt with by operative therapy. Where the condition is found in the upper urinary tract, the situation is not quite so satisfactory. Some palliation may be possible, apart from that afforded by the removal of a calculus. As constriction of the ureter is frequently present, and in any event the bulging cysts constitute undeniable obstacles to the free course of the urine, repeated ureteral dilatations, recommended by Kindall and followed by Hinman and ourselves, seem the logical procedure. Associated with dilatation, Kindall and Hinman advise the instillation of silver nitrate, in a 1 or 2 per cent solution.

If conservative measures fail, and renal insuffi-

ciency has developed, more radical procedures may be required, even the sacrifice of a kidney.

SUMMARY

The subject of pyelitis, ureteritis and cystitis cystica is reviewed.

The literature of the subject is briefly reviewed, and 10 cases of pyelitis and ureteritis cystica in which a clinical diagnosis was made are reported, including 2 observed by the author.

The genesis of the cysts is discussed and their evolution to cystitis glandularis is described.

These conditions are probably not so rare as previously thought.

The diagnosis of pyelitis cystica and ureteritis cystica is possible by urological study.

The treatment is discussed.

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DISCUSSION

DR. W. D. BIEBERBACH, Worcester: In 1933 a patient was admitted to the Urological Service at the Worcester City Hospital, at which time she was cystoscoped because of costovertebral tenderness, pain in the flank and hematuria. Following the cystoscopy the patient was greatly improved for three months, after which there was a recurrence of the hematuria. The peculiar shadow shown in her ureter presented a picture which was thought to be a papilloma or some similar growth. This finding plus the hematuria led to operation. At operation the ureter was apparently normal except for a distinct, fixed kink several centimeters below the ureteropelvic junction. Just below the kink, beady masses could be felt. In the ureter were found multiple growths with an appearance suggestive of papilloma. Because of this, ureteronephrectomy was decided on. The specimen showed multiple small cysts which studded the ureter and renal pelvis. I had the opportunity of recystoscoping this patient, and I might say that nothing was observed except inflammatory changes in the bladder. In 1936 there was the same appearance. I recystoscoped this patient recently and there was the same condition in the bladder. There were petechial spots in the wall of the bladder and on the trigone and dome. There were a few cysts that had the size and appearance of tapioca. I did a ureteropyelogram by injecting the pelvis with sodium iodide. I injected the ureter and pelvis with 10 cc. of the 7 per cent solution. It showed nothing of importance. There was a normal-appearing bladder. I then used a Woodruff catheter, which helped to bring out the vacuoles quite plainly. Of course we did not recognize this condition, which was identified by the pathologist. Probably if we had recognized it we should have treated it conservatively, as Dr. Patch has suggested.

DR. J. E. KERNEY, Providence, R. I.: I should like to ask Dr. Bieberbach if these cases of ureteritis cystica could not have been treated by desiccation of the cysts. I believe that in addition to the treatment outlined by Dr. Patch, it might be well to desiccate them.

DR. J. B. HICKS, Boston: While I was a member of the Lahey Clinic it was my privilege to do some 2000 cystoscopies. In this group I saw 2 cases that might be classified as cystitis cystica. The first patient, whom I saw ten years ago, was a woman thirty years old. There was no evidence of inflammation. She was treated by fulguration. She passed out of my care so that I was unable to follow her. The other case was that of a woman whom I saw in consultation with another doctor. She had been having painless hematuria for at least two years. Because of the hematuria, diagnoses such as stone, tumor and infection were considered. Cystoscopy showed definite evidence of bladder-neck obstruction. Urine cultures, sediments and guinea-pig inoculations were negative. Most of the time the urine was clear. The outstanding symptom was massive quantities of blood. The patient developed uremia and died. The presence of chronic inflammation in these conditions makes me think of infection as a possible etiologic agent. Possibly some of the viruses may be responsible for this condition. Dr. Patch did not mention tonight whether the urines were cultured in these cases. I should like him to bring this out.

DR. RICHARD CHUTE, Boston: I have never seen a recognizable case of ureteritis cystica. A few cysts in the bladder are very common. Offhand I can think of a half-dozen patients with a few cysts of the bladder.

DR. MYRON HAHN, JR., Boston: I have two small x-ray pictures here which I should like to show. The first is that of a man who came to the outpatient department complaining of pain in his back. The large cysts can be seen very plainly. One was protruding from the ureteral orifice. Puncturing these cysts relieved the backache. There was no operation. The patient returned to the clinic later, still without backache, and refused operation. The other picture brings out what Dr. Patch said about the condition at the lower end of the ureter, simulating

ureteritis cystica but actually due to a papilloma of the ureter. This appeared to be one of those tumors that responded well to radiation. After a preliminary course of radiation the patient was operated on. At operation the kidney tumor and ureter were removed. This was a case of tumor implants and not ureteritis cystica.

Dr. F. F. Weiner, Brockton: We have seen 2 cases of pyeloureteritis cystica at the Brockton Hospital. In one the patient was a woman of sixty whose chief complaint was hematuria. She was sent in for examination, and pyelograms were made. The diagnosis was very easy. The patient refused treatment because the symptoms stopped. There was an advanced condition of ureteritis cystica on one side, and a small number of vacuoles on the other. This emphasizes the bilaterality of the condition, which Dr. Patch has pointed out. The other case was that of a young man of twenty-three with hematuria and nothing else. In this case there were only three or four vacuoles in the kidney pelvis and upper ureter. We believed that the correct diagnosis was pyelitis and ureteritis cystica. We did nothing further because after his pyelography the patient had no further symptoms. I believe that palliative treatment was the proper procedure, because we do not know whether removing the kidney on that side would have prevented the occurrence of cysts on the other side. I also think that the other case was best handled conservatively. It was done three years ago and the patient is apparently in good health. She is getting along very well without further treatment.

Dr. William C. Quinby, Boston: The subject of pyeloureteritis cystica which Dr. Patch has presented so conclusively forms a definite pathologic picture, but one in which we must be careful not to confuse our thoughts, for the phenomenon of cystic formation is not a disease in itself but merely the pathologic response of the urinary epithelium to some antecedent cause. In my experience this cause has usually been a deep-seated pyelonephritis of bacterial origin. Therefore, in using the term "pyeloureteritis cystica" one does not describe a disease but merely a condition.

The epithelium of the urinary tract has the property of undergoing metaplasia as a result of various forms of stimuli. Furthermore, we are all familiar with the so-called bullous edema sometimes seen in the floor of the bladder as a result of obstructive changes of the return circulation without the presence of bacteria. I refer to the bullous edema around the ureteral orifice before the passage of a calculus. Similarly, in conditions of renal infection of long standing, the obstruction of perivesical lymph channels may be so continuous as to cause the formation of cysts which, owing to metaplasia, form an epithelial lining with active secretion, finally resulting in the picture of cystic ureteritis which Dr. Patch has described. In a few well-marked cases this cystic formation may be sufficiently extensive to cause mechanical obstruction in the ureter. But since all these ureters are somewhat dilated by the disease process, I do not see how further instrumental dilatation can bring anything more than transient relief. If permanent relief is to be achieved, one must be able to control the underlying cause, and this, as I have said, is usually a severe pyelonephritis — a condition in which cure is always difficult if not impossible. That an occasional cyst in the pelvis or ureter can be the cause of gross hematuria I very much doubt. Certainly bleeding cannot fairly be ascribed to such a condition unless every other source for it has been excluded.

Dr. Bieberbach: I should like to ask Dr. Patch about our 2 cases as regards the bacteriology. Both had clear urines, the cultures of the urine were negative and the sediments were negative. In the case of the woman, prior to operation she had an infection on the opposite side which was due to the staphylococcus. She got along satisfactorily with this cystic condition. In this case the condition was not secondary to infection. The kidney function was normal, dye appearing in four minutes. The blood nonprotein nitrogen was normal.

Dr. Ross Mintz, Boston: I should like to ask Dr. Patch whether he considers cystitis cystica and cystitis glandularis as pathological entities. Is cystitis cystica an end result, or is cystitis glandularis an end result of cystitis cystica?

Dr. Patch: It seems that my endeavor to summarize has caused confusion in the minds of some, and I am grateful to Dr. Quinby for clarifying the situation so ably, and drawing your attention to the fact that these different varieties of cystic inflammation are not clinical entities. This will appear quite clearly, I hope, in the published version of my paper.

With regard to the question as to the value of desiccation of the cysts, I should point out that this procedure does not deal with the underlying condition responsible for them, and therefore gives only temporary relief. In the presence of such a condition, the important considerations are the diagnosis of the underlying cause and its relief, whether it be calculus, obstructive factor or whatever condition is responsible for the chronic inflammation that has resulted in the cystic formations.

Ureteral dilatation does have a value in cases where the cystic accumulations in the ureter have obstructed the ureter, by producing an improvement in drainage through it. In cases where there is no obvious indication for operative interference, ureteral dilatation is to be recommended as a palliative measure. In several of the reported cases, as in one of ours, it was followed by definite improvement.

With regard to the frequency of these conditions of cystic formation, they occur much more frequently than is generally thought to be the case. In my paper, I quoted Morse, who found that cysts were present in the bladder of 17 per cent of 190 cases examined cystoscopically. In the bladder, its recognition is naturally easier than in the ureter or the kidney pelvis. I am convinced, however, that more careful study of pyelograms, and in particular more careful ureterography, will reveal cases which have formerly been overlooked.

Dr. Hicks asked a question as to the cultures in these cases. The bacterial flora is quite varied, but without any special significance.

Answering Dr. Quinby as to why these cases should bleed so freely, I am afraid that I cannot give a satisfactory explanation. That they do bleed at times, and very freely, is an undoubted fact. Frequently a diagnosis of tumor has been made and the kidney removed, and the true condition revealed by the pathologist. I have thought that obstruction to urinary outflow played an important role. Certainly ureteral dilatation has produced a definite improvement in my experience and that of others. I assume that dilatation effected a freer urinary outflow.

The obstruction of the ureters by the masses of cysts must have played a part in producing death in some of the cases. This is well shown in two of the Peter Bent Brigham cases in which uremia caused death and the lesions were discovered post mortem. In these cases, while there were other obstructive factors, the ureteral

blocks must have played a prominent part in the fatal ending.

I am convinced that if a careful watch is maintained, the conditions of ureteritis and pyelitis cystica will be found more frequently than in the past.

I lean very strongly to the view that a metaplastic process is responsible for the production of pyelitis, ureteritis and cystitis cystica, and that in its further development it may end in cystitis glandularis and even in malignancy.

THE INTRAMUSCULAR USE OF THE MONOETHANOLAMINE SALT OF CEVITAMIC ACID IN PATIENTS WITH VITAMIN C DEFICIENCY*

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REPEATED clinical and laboratory studies have demonstrated that the oral administration of pure cevitamic acid to the large majority of patients deficient in vitamin C causes a prompt amelioration of symptoms and a restoration of the vitamin C of the blood to normal concentration.[1, 2] In certain patients, however, who cannot tolerate cevitamic acid by mouth, or in whom gastric anacidity or the presence of pathologic changes in the bowel leads to destruction or poor absorption of the vitamin, the parenteral administration of vitamin C is an established clinical necessity.[2, 3] In such patients intravenous administration has been widely used. This route, however, is associated with considerable loss of the vitamin through the kidneys as the renal threshold is exceeded,[4, 5] and has the additional disadvantage of requiring venepuncture.

The intramuscular use of cevitamic acid seems to offer a method of escaping these disadvantages. This relatively strong acid, however, if given intramuscularly and not neutralized causes considerable sloughing of the tissues.[6] Neutralization by sodium hydroxide or bicarbonate gives an injectable substance readily absorbed and utilized.[6, 7] To make this preparation is time consuming, and requires considerable care if sterility is to be obtained without loss in potency. The monoethanolamine salt of cevitamic acid is a neutral salt and can be prepared so as to form a sterile stable solution.‖ This paper reports an investigation of the intramuscular use of this material in 3 patients with vitamin C deficiency, and compares its effect with the oral and intravenous administration of crystalline cevitamic acid.¶

METHODS

Patients were chosen for study who gave a history indicating marked reduction of vitamin C in their diet and who exhibited hemorrhagic manifestations of scurvy. Their blood showed a complete absence of the vitamin.

During the control period each patient was given a "house diet" free from citrus fruits. At the end of this period the twenty-four-hour specimen of urine and a sample of blood were analyzed and found to contain no cevitamic acid. Each patient was then given 1 gm. of vitamin C by mouth and the blood level of the vitamin was determined after a half, one and a half, two and a half, four and twenty-four hours. Urine was collected for the twenty-four-hour period after the administration of the vitamin; in 2 of the patients the first five-hour excretion was collected separately.

After the initial oral tolerance for vitamin C was concluded the patients were permitted to remain on the basic diet until the vitamin C was again absent from both blood and urine. The observations were then repeated following the intramuscular injection of 1 gm. of cevitamic acid in the form of the monoethanolamine salt. When the effects of this administration of the vitamin had disappeared, as shown by a return to approximately the same initial level of cevitamic acid in the blood, the observations were repeated after giving intravenously 1 gm. of crystalline cevitamic acid.

In 1 patient the therapeutic use of monoethanolamine cevitamate was attempted at a dosage of 100 mg. a day given intramuscularly for eight days. In this individual the observations following the oral administration of 1 gm. of cevitamic acid were repeated after the cevitamic acid level in the blood had reached a normal figure.

The urine was collected in dark bottles and kept on ice, acetic acid and chloroform being used as a preservative. The vitamin C present in the reduced form was determined by the method of Faulkner and Taylor.[4] The reduced cevitamic

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‖Supplied through the courtesy of the Abbott Laboratories, North Chicago, Illinois, and marketed under the trade name of Cenolate.

¶Supplied through the courtesy of Merck and Company, Rahway, New Jersey.

acid in the blood was determined by the method of Farmer and Abt.[8, 9]

RESULTS

Table 1 and Figures 1 and 2 show the data obtained for the 3 subjects studied. Following the oral administration of 1 gm. of vitamin C there was little change in the subnormal cevitamic acid levels of the blood of these patients. No vitamin was found in the urine during the twenty-four hours following ingestion of cevitamic acid. In 1 individual it was at first suspected that the absorption of the vitamin might have been impaired. Glucose-tolerance studies on this patient, however, revealed no abnormality of sugar absorption as measured by the form of the blood-sugar curve.

When 1 gm. of vitamin C dissolved in isotonic salt solution was given by vein there was a prompt rise of the blood level of the vitamin, followed by marked excretion into the urine as the renal threshold for the vitamin was exceeded. In confirmation of the observations of Wright, Lilienfeld and MacLenathen,[10] the excretion occurred chiefly in the first five hours. The twenty-four-hour excretion of cevitamic acid ranged between 174 and 265 mg., or between 17 and 27 per cent of the amount of vitamin given.

Following the intramuscular administration of 1 gm. of cevitamic acid in the form of the monoethanolamine salt, there was again a prompt rise in the blood level of cevitamic acid. The rise was not so great as that which followed the intravenous administration of the vitamin, and the loss in the urine was much less. From 60 to 140 mg. of cevitamic acid, or between 6 and 14 per cent of the amount of the vitamin injected, was excreted in the urine during the twenty-four hours following administration. Most of this excretion occurred in the first five hours following administration. The rate of rise in the blood level of the vitamin indicated a good rate of absorption.

One patient (Case 3) was saturated by the daily

TABLE 1. *The Effect of Route of Administration of 1 Gm. of Vitamin C on the Concentration of Cevitamic Acid in the Blood and Urine.*

Case No.	Plasma Cevitamic Acid Content				Urine Cevitamic Acid Excretion			
	Hours after administration	Method of administration: Oral	Intramuscular	Intravenous	Hours after administration	Method of administration: Oral	Intramuscular	Intravenous
		mg. %	mg. %	mg. %		mg.	mg.	mg.
1	0 (control)	0	0	0.17				
	½	0	2.56	3.21	5	—	—	—
	1½	0.07	2.48	1.70				
	2½	0.18	2.13	1.50				
	4	0.20	1.52	1.22	24	0	140	174
	24	0	0.12	0.36				
2	0 (control)	0	0	0.25				
	½	0	1.23	3.65	5	0	57.2	237.5
	1½	0.33	1.98	2.21				
	2½	0.51	1.66	2.86				
	4	0.52	0.66	0.98	24‡	0	60.1	237.5
	24	0	0.43	0.40				
3*	0 (control)	0	0	0.12				
	½	0	0.73	6.24	5	0	70.1	200.2
	1½	0.15	1.72	3.28				
	2½	0.23	1.86	2.09				
	4	0	1.50	1.27	24‡	0	98.2	264.9
	24	0	0.37	0.83				
3†	0 (control)	0.81						
	½	0.71			5	2.7		
	1½	1.14						
	2½	1.60						
	4	1.77			24‡	115.8		
	24	1.19						

*Tests conducted during deficient state.
†Oral test repeated after saturation with 100 mg. of monoethanolamine cevitamate intramuscularly daily for eight days.
‡24-hour values include five-hour values.

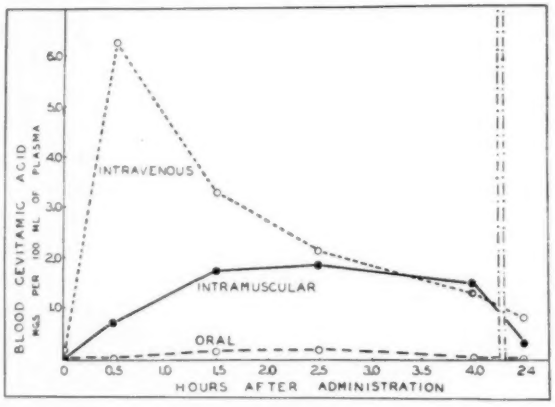

FIGURE 1.

The effect of route of administration of 1.0 gm. of vitamin C on the concentration of cevitamic acid in the blood plasma of a patient (Case 3) with vitamin C deficiency.

intramuscular administration of 100 mg. of cevitamic acid as the monoethanolamine salt. In eight days the blood level rose from 0.12 to 0.81 mg. per 100 cc. of blood plasma. The oral administration of 1 gm. of vitamin C at this time showed a prompt rise in the blood plasma cevitamic acid to 1.77 mg. per 100 cc. Data for the two oral tolerance

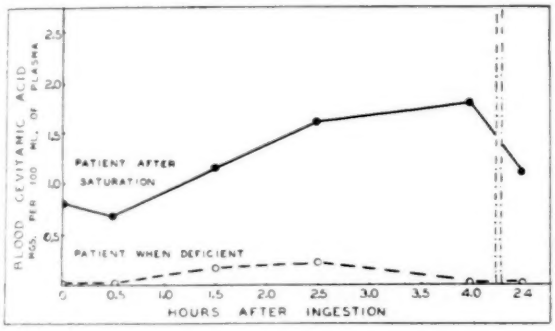

FIGURE 2.

The effect of the oral administration of 1.0 gm. of vitamin C on the concentration of cevitamic acid in the blood plasma of a patient (Case 3) with vitamin C deficiency, before and after saturation with the intramuscular administration of 100 mg. of monoethanolamine cevitamate daily for eight days.

tests are summarized in Table 1, and the curves are shown in Figure 2. One hundred and sixteen milligrams of cevitamic acid was excreted into the urine during the twenty-four hours following the ingestion of the vitamin C, the largest amount being excreted between the sixth and the twenty-fourth hours.

Eleven intramuscular injections of a solution of the monoethanolamine salt of cevitamic acid in doses ranging between 0.1 and 1.0 gm. were given, without any immediate or delayed, local or systemic reactions.

CONCLUSIONS

The intramuscular injection of the monoethanolamine salt of cevitamic acid presents a simple and effective way of administering vitamin C parenterally when need for this type of injection is indicated.

There were no immediate or delayed, local or systemic reactions following its use in the 3 patients studied.

Its intramuscular administration was followed by a prompt increase in the vitamin C of the blood. The loss of vitamin C in the urine was not so marked as when crystalline cevitamic acid was given intravenously.

A patient with marked vitamin C deprivation was saturated in eight days by the daily intramuscular injection of 100 mg. of cevitamic acid as the monoethanolamine salt.

We are indebted to Miss Nancy Marean for technical assistance.

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METRAZOL TREATMENT OF DEPRESSIONS*

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WORCESTER, MASSACHUSETTS

ON THE basis of the data published by Low et al.,[1] which indicated favorable results with Metrazol therapy in the affective psychoses, in 1938 we began an investigation of a group of 20 depressed women patients at the Worcester State Hospital. The purpose of this paper is to indicate the results obtained and to describe certain phenomena observed in the course of the treatments. Within recent months several reports have appeared in the literature. Low states that 13 of his 16 treated manic-depressive patients recovered; Bennett[2] announced uniformly good results in 21 cases; Cook[3] called his 4 recoveries in 5 cases promising and dramatic; and Serko[4] cited 2 cases with recovery.

The rationale of Metrazol therapy in depressed states is at present unknown. Bennett[2] has stated that the effects are probably due to the ability of the treated patient to prove to himself his willingness to undergo punishment, with subsequent resolution of guilt and lifting of the depression. The various theories underlying the modus operandi of Metrazol which have been advanced by Von Meduna,[5] Friedman[6] and Gellhorn[7] in the treatment of schizophrenia may or may not be applicable to the treatment of the depressions. It is beyond the intention of this report to enter this controversial field.

METHOD

Prior to the beginning of treatment all patients were examined in order to determine any physical disability contraindicating treatment. Laboratory examinations included x-ray examination of the chest and blood and urine studies. The finding of a systolic blood pressure over 150 mm. of mercury, a diastolic blood pressure over 90 mm., marked retinal arteriosclerosis, impaired cardiac function or any febrile illness was each considered as a contraindication.

Metrazol (Bilhuber-Knoll) was administered intravenously in 10 per cent aqueous solution; the initial dose was 3 cc., which was increased by 1-cc. increments until the convulsive threshold was reached. The dose was further increased by 1-cc. amounts when tolerance to the drug, as manifested by the absence of the grand-mal seizure, developed during the course of treatments. Doses were given three times weekly, not less than one hour following and one hour preceding meals. They were continued until remission occurred. In 3 cases treatments were discontinued after the apparent maximum improvement had been attained.

The greatest improvement following individual treatments seemed to occur after seizures of the grand-mal type. After seizures of the petit-mal, abortive-tonic or confusional type, many patients became more agitated and apprehensive.

No formal psychotherapy was administered during the course of treatment. However, reassurance was necessary from time to time for some patients in order to allay apprehension regarding the treatments.

The only complication encountered was occasional bilateral dislocation of the mandible, which was usually reduced spontaneously after relaxation of the muscles. It is our opinion that careful nursing procedure during and immediately following the seizure is the most important factor in reducing the possibility of fractures and dislocations which may occur during the course of therapy. Two nurses were employed during each seizure to hold the patient in such a way as to prevent abduction at the hips and shoulders.

CLINICAL MATERIAL AND RESULTS

Of the 20 patients treated, those who were between forty and sixty years of age and who had had no previous attacks of mental disorder were classified as involutional psychoses. When paranoid ideas were prominent these patients were considered to be of the paranoid type; otherwise they were considered to be of the melancholic type. Those patients below forty, and also those who had had previous attacks of mania or depression, were considered as having manic-depressive psychoses. All were of the depressed type. There were 3 castrates (Cases 1, 3 and 7), and 6 patients (Cases 4, 5, 10, 11, 12 and 18) were known to have passed through the menopause. The duration of mental illness prior to the institution of treatment ranged from two months to five years. Some of these patients had been treated with amphetamine (Benzedrine), Progynon, Emmenin or Theelin with no noteworthy effects; these treatments had been discontinued at least three months before treatment with Metrazol was begun.

The essential data concerning these patients, the

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nature of the Metrazol treatment and the clinical results are presented in Table 1. The time which has elapsed since treatment was discontinued varies from one to five and a half months, the average period being three months.

DISCUSSION

Of the 20 patients treated, 17 (85 per cent) had complete remission of symptoms and 3 (15 per cent) manifested definite improvement. Of the 3 patients who underwent no remission but did improve, all were over fifty years of age, and 2 had minimal retinal arteriosclerosis. There was no correlation between the duration of illness prior to the institution of treatment and the degree of success. In the 3 patients who did not have a remission, the duration of illness ranged from eight months to five years. There was no correlation between the age of the patient or the duration of illness and the number of treatments required to produce a remission.

Motor activity was the first symptom to become normalized in all cases except Cases 4, 7 and 14, in which all symptoms disappeared suddenly. Agitated patients became quiet and obvious tenseness disappeared; retarded patients became sufficiently active to participate in productive work. Following the return to a normal degree of activity the mood lifted — in some cases suddenly and completely, in others for increasingly longer periods of time following seizures. Delusions and delusional ideas were in all cases the last of the symptoms to disappear, and were put forward by the patients with diminishing conviction as treatment progressed.

The patients who underwent remissions were able to return at once to their previous occupations. Information concerning them was obtained by monthly interviews and correspondence after their discharge from the hospital. One patient (Case 12) returned voluntarily for a second course of treatments, stating that on resuming a difficult domestic situation she noted recurrence of depression and feelings of guilt; she again underwent a full remission. With this exception all patients stated that there had been no return of their former symptoms. Tension and anxiety were at times manifested during the interviews following remission, when some patients discussed certain phases of their personal life. These states were, however, readily overcome by the patients themselves before the termination of the interview. This material had not been expressed during the psychosis. No emotional reaction was evidenced in discussing ideas expressed during the acute period of the psychosis.

During the course of treatments, 7 patients (Cases 4, 5, 8, 11, 14, 16 and 19) had somatic complaints, for example backache, pains in the joints, palpitation, weakness, epigastric pain, prick-

TABLE 1. *Clinical Effect of Metrazol Treatment in Depressions.*

DIAGNOSIS	CASE	AGE	PREVIOUS ATTACKS	DURATION OF ILLNESS	PREVIOUS TREATMENT	NO. OF METRAZOL TREATMENTS	NO. OF SEIZURES	MAXIMUM DOSE	RESULT
		yr.		yr.				cc.	
Involutional psychosis (paranoid type)	1	52	0	2	Amphetamine	6	5	4	Remission
	2	46	0	5	0	13	7	8	Remission
	3	46	0	2	Progynon Amphetamine	19	14	7	Remission
	4	54	0	2/3	0	20	10	8	Remission
	5	52	0	4 1/2	Emmenin	40	34	5	Improved
	6	43	0	3 1/2	Photodyne Progynon	9	6	7	Remission
Involutional psychosis (melancholic type)	7	49	0	1 1/4	Emmenin	5	5	3	Remission
	8	41	0	1 3/4	0	11	3	9	Remission
	9	45	0	2 1/2	0	17	6	8	Remission
	10	56	0	1/6	0	13	10	7	Remission
	11	55	0	2/3	Amphetamine	23	11	9	Improved
	12	50	0	1/6	0	1	1	3	Remission
						8	3	7	Remission
	13	54	0	2	0	9	4	7	Remission
Manic-depressive psychosis (depressed type)	14	40	0	3 1/2	Theelin Amphetamine	16	10	6	Remission
	15	28	0	1/2	Progynon	3	3	3	Remission
	16	42	2 (depressed)	2	Progynon Amphetamine	13	6	7	Remission
	17	32	3 (depressed)	1/2	0	2	1	3	Remission
	18	59	2 (depressed) 1 (manic)	2/3	0	9	7	4	Improved
	19	45	5 (depressed)	1 1/2	0	12	7	8	Remission
	20	36	1 (manic)	1 2/3	0	14	11	7	Remission

ling sensations in the scalp and blurred vision. Physical, x-ray and ophthalmoscopic examinations gave no evidence of any somatic basis for these symptoms. It was noted that these complaints were more numerous following seizures of the petit-mal or confusional type, and were less frequent or absent following seizures of the grand-mal type. The complaints made their appearance as the depression lifted and as the ideas of guilt or persecution diminished, and in every case had disappeared by the time remission had occurred. It seemed possible that repressed material was being symbolically expressed in the form of somatic symptoms.

During the course of therapy, 6 patients (Cases 4, 10, 14, 16, 19 and 20) complained of loss of memory for certain material. However, examination revealed that there was no memory defect, and that some of the patients were apparently complaining of inability to concentrate; many of the patients showed, however, considerable affectivity when some of the "forgotten" ideas were recalled, indicating that they might have been wishfully forgetting (repressing) this material.

SUMMARY

Metrazol therapy was carried out in a group of 20 depressed women patients, classified as having involutional and manic-depressive psychoses. The age range was twenty-eight to fifty-nine, and the patients had been ill from two months to five years. Treatments were administered three times weekly beginning with a dose of 3 cc. of 10 per cent aqueous solution of Metrazol, which was increased as necessary to obtain typical grand-mal seizures; the treatments were discontinued when remission or considerable improvement had taken place. In this series, 17 patients underwent full remission of symptoms and 3 manifested improvement. The order of disappearance of psychotic symptoms is described and certain clinical features associated with this form of treatment are discussed. These results indicate that further trial with Metrazol is warranted in the treatment of depressions of these types.

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CALCIFIC AORTIC STENOSIS—A CLINICAL ENTITY

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THE last decade has witnessed notable advances toward the fuller recognition of calcific aortic stenosis as a clinical entity. Data have been assembled producing a picture so characteristic that an increase in the frequency with which this diagnosis is correctly made may be expected. When it is appreciated that several other entities, including angina pectoris and coronary thrombosis, may be simulated by calcific aortic stenosis, its importance from a practical as well as an academic view can be seen.

HISTORY

Although Mönckeberg[1] is justly credited with the first comprehensive pathological identification of calcific aortic stenosis and Christian[2] is similarly credited for emphasizing it as a clinical entity, the older literature abounds with cases of calcific aortic stenosis with typical clinical pictures. Cases are found in which, despite incomplete data, the diagnosis could very reasonably have been made had the present-day improved clinical methods been available. Thus, Boneti[3] in 1700 stated that Rayger in 1672 reported sudden death in a patient with calcific aortic cusps. Lloyd[4] in 1846 reported sudden death in a man of fifty-three with calcific aortic stenosis and a hypertrophied heart. Gautier[5] in 1860 reported sudden death in a boy of twelve with calcific aortic stenosis and a normal mitral valve. Peacock[6] reported sudden death in a man of twenty-three who had calcific aortic stenosis and aortic insufficiency with a hypertrophied heart. Budin and Decaudin[7] reported a woman of forty-eight who died suddenly; they noted calcific aortic stenosis and aortic insufficiency with thickened,

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fused, calcific valve cusps. Wilks and Moxon[8] as early as 1875 called attention to the connection between aortic stenosis and sudden death.

The morbid anatomy of aortic stenosis has received much detailed study, dating especially since 1904, when Mönckeberg's[1] classical paper defined the pathologic alterations produced in this condition. Since then notable studies in this field have been made by Margolis, Ziellessen and Barnes,[9] Sohval and Gross,[10] Lesnick and Schlesinger[11] and Clawson et al.[12]

Christian[2] predicted the possibility of the x-ray demonstration of cardiac calcification in vivo, and recently Sosman and Wosika[27] first reported such a case.

In the field of clinical physiology, the pulsus tardus et parvus was long recognized by the older writers. Recent contributions concerning the physiology and hemodynamics of aortic stenosis have been made by Eyster, Meek and Hodges[13] in 1927, Katz, Ralli and Cheer[14] in 1928 and Green[15] in 1936.

Important summaries of extended clinical observations of calcific aortic stenosis have been published by Contratto and Levine,[16] McGinn and White,[17] Willius[18, 19] and Willius and Camp.[20]

Etiology

Campbell and Shackle[23] investigated the etiologic factors in 296 cases of all types of aortic valvular disease. They found that acute rheumatism accounted for 200 cases, syphilis for 55, atheroma for 20 and all other causes for 21. Contratto and Levine[16] reviewed 180 cases of aortic stenosis and found a definite history of rheumatic fever in 57 (32 per cent). They believe that many additional cases could have been classified in this latter category if more careful histories had been elicited and if patients could have more readily recalled minor yet typical rheumatic episodes early in life. They concluded that rheumatic fever is the most frequent and most important cause of aortic stenosis.

Uniformity of opinion concerning the etiology of calcific aortic stenosis as distinct from aortic stenosis in general has not yet been reached. Mönckeberg[1] believed the former to be a degenerative disease with a resulting deposit of calcium. Cabot[21] acknowledged infection as a factor but believed the nature of the infectious process to be different from that occurring in the presence of rheumatic valvular disease. Margolis, Ziellessen and Barnes[9] claimed an inflammatory basis in some cases and a degenerative process in others. Boas[22] believed calcific aortic stenosis to be rheumatic in origin. Sohval and Gross[10] in their close study of calcific sclerosis of the aortic valve concluded that the disease was purely degenerative showing practically none of the stigmas of rheumatic activity. They suspected that the process depended on individual predisposition to collagen involution and deposition of lipoid and calcium.

Christian[2] has been impressed with the frequent history of rheumatism in early life, and, contrary to his own view in 1928,[28] now thinks that the lesion is rheumatic in origin. Mallory[24] believes that calcareous aortic stenosis is very rarely rheumatic in origin. Although Willius[18] holds that the process is inflammatory, its exact nature still being unknown, he points out the following factors against rheumatic fever as the etiologic agent: the overwhelming predominance of the disease in men relatively late in life; the low incidence of rheumatic fever (21 per cent of 77 reported cases); and the rarity of pericardial involvement. As an argument against an atherosclerotic genesis he called attention to the remarkable paucity of atherosclerosis in portions of the cardiovascular system other than the valve leaflets, annulus and a small contiguous portion of the aorta. It is generally conceded that the relative freedom from atherosclerosis in the supravalvular portion of the aorta may be due to the protection afforded by the low pressure effected by the calcific aortic stenosis. Berk and Dinnerstein[25] on the basis of their study concluded that the etiology is still unknown but favored the possibility of a primary degeneration. Other findings which militate against the possibility of rheumatic etiology may be cited: the solitary occurrence of the lesion, that is, the absence of involvement of the mitral valve; the lack of appreciable thickening or shortening of the chordae tendineae; the massive deposits of calcium; and the absence of Aschoff bodies in the myocardium. Against arteriosclerosis, on the other hand, may be cited the absence of any marked sclerotic changes elsewhere in the body. Lesnick and Schlesinger[11] in a study of 39 cases of calcific aortic stenosis found 17 to have no associated mitral deformity and 22 to have an associated deformity of the mitral valve of rheumatic origin. They concluded that calcific aortic stenosis was not always rheumatic in origin, but thought that in some cases the underlying etiologic factor was probably of the nature of an arteriosclerotic degeneration. Clawson, Noble and Lufkin[12] concluded from a study of 200 cases that calcific aortic stenosis was the commonest healed aortic lesion and that the change in the valve was due to repeated attacks of rheumatic proliferative inflammation with calcification similar to that commonly seen in mitral cusps.

The decision concerning the etiology must depend finally on thorough examination of the heart for the presence of rheumatic stigmas.

The hypothesis that calcific aortic stenosis represents the healed stage of subacute bacterial endocarditis usually fails to find corroboration in the absence of a history of prolonged febrile illness and in the lack at necropsy of healed embolic visceral lesions.

Incidence

Calcific aortic stenosis occurred[17] in 1.8 per cent of 6800 autopsied cases or 2.3 per cent of 4800 autopsied cardiovascular-disease cases.

Age and Sex

The combined data of several investigators[20, 11, 6, 16] showed 180 men (67.9 per cent) affected in a total of 265 cases. The same data revealed the greatest incidence in the middle and older age groups. In one series[16] the average age in 180 cases was fifty-two years and six months.

Morbid Anatomy

Mönckeberg[1] believed that the anatomical alterations in calcific aortic stenosis were due to primary sclerocalcific changes. He regarded the process as originating in small atheromatous plaques situated in the sinus pockets, and believed that these plaques increased in extent and ascended toward the free border of the valve. He appreciated the necessity of differentiating the process from results of rheumatic fever, pointing out an important feature; namely, that the sclerotic and calcific process is largely present in the fibrosa layer of the aortic valve, whereas when it occurs as a secondary process in rheumatic fever it is confined chiefly to the ventricularis layer.

Willius[18] demonstrated that calcific aortic stenosis is usually limited to the cusps themselves. Variable amounts of calcareous material are deposited, primarily involving the aortic annulus, frequently one of the valve commissures and valve leaflets, although the free margin of the leaflets is involved chiefly when the process is very extensive. Fusion of the leaflets tends to occur, producing an adynamic valve which results in a barrier where stenosis predominates, but lesser degrees of aortic insufficiency may also be present. The calcareous process rarely involves the aorta itself except the immediately contiguous segment, and never involves the region where the coronary arteries originate. The left ventricle undergoes hypertrophy. An associated pericarditis is rare.

Sohval and Gross[10] made an extensive study of the anatomy of calcific sclerosis of the aortic valve (Mönckeberg type). They found:

> The valves are transformed into stiffened irregular nodular leaves with most of the thickening taking place throughout the body of the leaflets rather than at the free edge. In advanced stages secondary sclerotic transformation produces extraordinary and bizarre deformities. Nodules vary in extent, extremely hard and rounded or sharply irregular, often penetrating through the ventricularis and auricularis enveloping layers of the cusp. Commissural agglutination may be sharp in milder forms and in advanced forms may be broadened, nodular and distorted, thus differing from the evenly rounded and broadened lesions often seen in subacute bacterial endocarditis, as well as from the delicate, grooved agglutinations found in the pure rheumatic process. The edges of the aortic leaflets in Mönckeberg's sclerosis may be sharp, or thickened and distorted, and do not usually present the rolled and inverted gross configurations characteristic of the rheumatic lesion. Histologically the earliest change is seen in the fibrosa layer near the base of the leaflet. Sclerotic and hyalin changes followed by lipoid changes occur. Next there is a deposition of calcific material. The nuclei in the fibrosa collagen tend to disappear. Capillarization of the aortic ring may occur if the process is close to the ring. In contrast to this the rheumatic calcified valve presents thickening and often vascularization of the spongiosa and ventricular layers in which calcification also occurs. Lesions of the valve ring are almost invariably present.

Sohval and Gross[10] believed that the pathogenesis of Mönckeberg's sclerosis was purely and primarily degenerative in character, showing practically none of the characteristics of rheumatic activity. They thought that the process probably depended on an individual predisposition to collagen involution and deposition of lipoid and calcium.

Berk and Dinnerstein[25] found involvement of the aortic ring, primarily at the roots of the valve. In the first stage only the outer layer at the site of the sinus of Valsalva was affected. Calcification then extended into the leaflets or one of the commissures, bulged into the sinuses of the valves, or formed radiating buckles within the valves themselves. Deposits of lime salts often filled the sinuses completely. The condition frequently progressed into the ventricles, producing spur-like formations under the endocardium. They found that calcification of the aortic valve might occur in combination with calcification of the annulus fibrosus or might be entirely isolated. The valves themselves were thickened, had an irregular surface and were fused at the commissures. The places of fusions often shrunk considerably and in so doing usually caused stenosis of the valves.

Margolis, Ziellessen and Barnes[9] found a tendency to hyalinization of the connective tissue with a deposition of lipoid material in the aortic valve ring and in the aortic valve with subsequent calcification. They believed that some cases had an inflammatory, others a degenerative basis. Ischemia, due to diminution of the vascular supply of the

affected tissues, seemed to be the basic pathogenic factor, producing hyalinization and other degenerative changes which subsequently proceed to calcification. The diminished blood supply might be due to narrowing or possibly obliteration of the arterioles of the aortic valve ring either as a part of generalized arteriosclerosis or as a selective and localized process, degenerative and calcareous deposits in the valves thus being produced.

Boas[22] alluded to the occasional extension of the fibrosis and calcification from the aortic ring to the annulus fibrosus and to the interventricular septum, with frequent impingement on and replacement of the atrioventricular bundle; such a change produced an anatomical basis for conduction defects in patients with calcific aortic stenosis.

Physiology

Eyster, Meek and Hodges[13] found that experimental aortic stenosis and insufficiency in dogs were usually associated with a gradually developing cardiac hypertrophy. The heart with aortic insufficiency before hypertrophy developed failed to react as effectively to an overload as did the normal heart. There were no electrocardiographic changes characteristic of the early dilatation or hypertrophy subsequent to aortic lesions. Even extreme degrees of dilatation in the normal heart failed to cause significant changes in the electrocardiogram.

Katz, Ralli and Cheer[14] recorded the cardiodynamic changes in the aorta and left ventricle due to stenosis of the aorta by means of simultaneous pressure curves from the left ventricle and aorta. The disappearance of the similarity of the basic form of the two pressure curves during ejection when the aorta was stenosed arose from the fact that the two chambers were no longer in free communication while blood was being ejected. The faster and larger rise in ventricular pressure during ejection as compared with the slower and smaller rise in aortic pressure, was due to the decrease in the rate of conversion of potential mechanical energy in the ventricle to kinetic energy of flow. The lowering of the aortic pressure levels and the decrease in pulse pressure were due to the diminution in systolic discharge and minute output of the heart — obviously caused by utilization of more of the mechanical energy of the ventricle so as to overcome the added obstruction caused by the stenosis. In marked stenosis the effect of the increase in diastolic stretch may be large enough to counterbalance the primary effect of the aortic constriction and cause a temporary rise in pressure levels.

Green[15] found a decrease in coronary flow mainly during systole in aortic stenosis, and believed that it caused a relatively high degree of systolic peripheral coronary resistance in relation to aortic pressure.

Boas[22] thought that when the aortic orifice was greatly narrowed, rapidly developing heart failure, by still further retarding the blood flow through the minute opening, might induce an acute myocardial ischemia analogous to that following coronary artery thrombosis and give rise to identical symptoms.

Harrison, quoted by Contratto and Levine,[16] believed that the angina might be due to relative anoxia. The work done by the heart demands more oxygen than the coronary blood flow can provide. The intraventricular pressure must be enormously increased because of aortic stenosis. The velocity factor, which under usual conditions has relatively little to do with cardiac work, may become the greatest factor in aortic stenosis, when with a markedly narrowed orifice the rate of flow must be enormously greater during systole. Angina may also be due to slight vasomotor changes in the caliber of the normal coronary vessels often found in cases of calcific aortic stenosis in young people. This may account for the less frequent relation of exercise to pain than in the ordinary coronary stenosis cases with angina pectoris. Contratto and Levine suggested a suction-pump action of the aortic blood stream with its increased velocity on the orifices of the coronary arteries which leave at right angles; this possibly diminishes the coronary blood flow and leads to a relative myocardial ischemia.

Diagnosis

Symptoms

The diagnosis of calcific aortic stenosis can only rarely be made on the basis of subjective findings. The heart is apparently able to compensate well for the change in dynamics caused by aortic stenosis. The relatively few subjective symptoms, coupled with general lack of awareness of this entity, have in the past led to errors in diagnosis of this form of valvular disease. In one series of 42 cases[20] only 6 had cardiac complaints. In another series of 236 cases[17] only a third were diagnosed ante mortem.

The chief complaints are usually those associated with angina pectoris, left ventricular failure (cardiac asthma), syncope, Adams-Stokes syndrome or congestive heart failure.

Angina Pectoris. The symptoms of angina pectoris are found in a varying but considerable percentage of patients with calcific aortic stenosis. McGinn and White[17] reported that 19 per cent of 236 patients had angina pectoris. Margolis et al.[9]

reported 42 cases, 4 having angina pectoris. Contratto and Levine[16] reported 41, or 23 per cent, of 180 cases as having well-defined angina pectoris. Boas[22] reported 4 of his 19 cases as having classic angina pectoris. In all these cases a relative myocardial ischemia was the apparent cause.

Left Ventricular Failure. Either a sudden or gradual failure of the left ventricle causes dyspnea, so-called "cardiac asthma," due to the diminished blood flow with congestion in the lungs. Although this manifestation is relatively rare, it should arouse suspicion of the presence of calcific aortic stenosis, particularly in the older age groups.

Syncope and Sudden Death. Among the earliest cases of calcific aortic stenosis in the literature are found those with syncope and sudden death. Marvin and Sullivan[26] reviewed this literature, and pointed out that sudden death may occur in aortic stenosis as well as in the more widely recognized conditions of coronary thrombosis, anginal heart failure, atrioventricular block and syphilitic aortitis with aortic insufficiency. They believed the syncope to be due to overactive carotid-sinus reflex. This hypothesis does not find corroboration in the results of other investigators.[16]

Adams-Stokes Syndrome. Typical Adams-Stokes attacks may occur in the course of calcific aortic stenosis. Their presence should be looked for when this diagnosis is under consideration. The attacks are apparently caused by the relative cerebral anemia due to the slow ventricular rate, or actual temporary cardiac asystole.

Congestive Heart Failure. The slow progressive nature of the lesion in calcific aortic stenosis produces symptoms of congestive heart failure relatively late in the course of the disease.

Signs

Blood Pressure. A review of the data on blood-pressure readings reveals that when no complicating factors are present calcific aortic stenosis produces a systolic pressure which is likely to be low and a diastolic pressure which is apt to be slightly elevated, resulting in a small pulse pressure. Other factors which influence the height of the blood pressure are associated essential hypertension and, more often, aortic insufficiency. In 180 cases reported by Contratto and Levine[16] an average systolic pressure of 145 and diastolic pressure of 84 were noted. The range of the systolic pressures was from 260 to 80, while the diastolic pressures varied from 156 to 10.

Pulse. The pulse is characteristically small, of a plateau type and not infrequently slow. It has been described as anacrotic or bisferious.

Murmurs. There is a characteristic long, loud, rough systolic murmur, either localized in the aortic area or, as often occurs, transmitted to the vessels of the neck. The diastolic murmur of a complicating aortic insufficiency is occasionally present. An Austin-Flint murmur may rarely be heard. In the interpretation of heart sounds it must be borne in mind that murmurs heard over the aortic or pulmonic areas do not necessarily arise from the corresponding valve.

Second Aortic Sound. Owing to the adynamic aortic cusps found in calcific aortic stenosis, the second aortic sound is frequently of diminished intensity and may be entirely absent.

Thrill. A systolic thrill over the aortic area is often found in calcific aortic stenosis. However, it is not consistently present and must not be insisted on before the diagnosis is made. In one series of 51 cases of aortic stenosis that came to necropsy a thrill had been found in only 21.[17]

Enlargement of the Heart. As a result of the obstruction to the free passage of blood through the aortic orifice because of calcific aortic stenosis, it has been shown[13] both clinically and experimentally that the heart undergoes a gradual hypertrophy which is preceded by a stage of initial dilatation. In cases of long standing a markedly enlarged heart is the usual finding. Chevers[29] pointed out as long ago as 1842 that a morbid narrowing of the aortic orifice caused cardiac hypertrophy even in the presence of a completely obliterated pericardium.

Electrocardiogram. Defects in conduction are commonly found in electrocardiograms. These include typical cases of bundle-branch block, increased P-R intervals and cases of complete heart block. Recently it has also been shown[22] that ischemia of the myocardium in calcific aortic stenosis, which may be further increased by a slow ventricular rate, produces electrocardiographic changes indistinguishable from those characterizing thrombosis of the coronary artery. Boas[22] pointed out an anatomical basis for conduction defects in cases with calcific aortic stenosis. Master, Jaffe and Dack[30] recently reported an electrocardiogram which could not be differentiated from that encountered in coronary thrombosis.

X-ray and Fluoroscopy. Sosman and Wosika[27] reported 23 cases and concluded that roentgen-ray visualization, roentgenoscopically and roentgenographically, of calcified heart valves during life was possible with present-day roentgen apparatus. With the proper technic[25, 27] the calcified valve can be seen to produce small dense shadows, rapidly moving or dancing up and down. They cannot be projected outside the cardiac shadow and

are not affected by deep inspiration. It appears that they are best seen in the right oblique view in the median line, or a little to the right of it in the lowest third of the cardiac area.

Course

The slow, progressive nature of the pathologic process similarly produces a prolonged clinical course. Symptoms do not appear until relatively late in the disease. When these have once made their appearance the subsequent course is usually brief. Thus, cardiac failure and often sudden death may be looked for. A life expectancy of about one year is the usual outlook when symptoms of congestive heart failure are noted.

TREATMENT

The therapy of aortic stenosis prior to the advent of symptoms of congestive heart failure must be aimed at restricting the patient's activities and instituting a highly individualized regime in order to avoid unnecessary overwork of the heart.

When congestive heart failure makes its appearance it must be treated as failure due to any other type of lesion.

CONCLUSIONS

Calcific aortic stenosis is becoming more and more often recognized. The possibility of its presence in an aortic lesion when no mitral lesion is present should be borne in mind.

The condition is not uncommonly followed by sudden death, and Adams-Stokes attacks may occur.

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REPORT ON MEDICAL PROGRESS

THORACIC SURGERY

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ANESTHESIA

IN THORACIC as in general surgery, there exists no unanimity regarding the choice of the anesthetic agent or the technic of administration. Local anesthesia for extensive operations on the chest wall or lungs has never been widely used in this country but remains the method of choice for the less extensive operations of drainage for empyema or lung abscess. Cyclopropane and oxygen has come into vogue in recent years, and in many clinics is considered indispensable for chest surgery. Certainly this mixture is preferable to nitrous oxide and oxygen because of its higher content of oxygen. However, the circulatory apparatus is under a severe strain in many chest operations, and the toxic effects of cyclopropane on the heart have not been tested by experience.

An ether vapor and oxygen mixture is, theoretically at least, even more ideal than cyclopropane in preventing anoxemia, as the oxygen content may be raised to almost 100 per cent. The reviewer has for several years been on the alert for any evidence that warm ether vapor mixed with oxygen and properly administered possesses irritating qualities deleterious to the lungs or air passages. It has been used as the anesthetic of election in hundreds of cases of thoracic disease, including acute tuberculosis. It has been compared with avertin, cyclopropane, barbiturate sedation and other agents singly and in combination. No evidence has been found that ether possesses undesirable qualities for use in chest cases, and unless special circumstances exist it is considered preferable to any other existing anesthetic. The prejudice against ether found its origin in the days of cone administration when patients were permitted to gurgle in their secretions in a state of sublethal asphyxia.

Experienced thoracic surgeons insist on differential-pressure anesthesia for operations in the free pleural cavity, although they are ready to admit that many patients will survive such an operation without it. Tracheal intubation has largely replaced the tightly fitting mask in the technic of administration. For differential pressure alone, a tube entering the larynx via the nose is sufficient; if purulent secretions are plentiful, as in bronchiectasis, a large Flagg tube is employed so that aspiration can be carried on. In some clinics (Rienhoff, Ochsner) intubation of the trachea is avoided on the ground that infection may be introduced.

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BRONCHOGRAPHY

Roentgen-ray demonstration of the bronchial tree by the injection of opaque solutions into the respiratory tract is an established and exceedingly valuable procedure. If carefully done by an expert untoward results are rarely encountered. The value of the demonstrations as a preoperative study for the visualization of pathologic lesions transcends its use in pure diagnosis.

The use of bronchography should not be considered comparable to that of contrast mediums in the study of the gastrointestinal tract. In general it requires a more exacting technic, and if used incorrectly the oil may be retained in the parenchyma of the lung and obscure later pathologic developments.

The chief use of bronchography has been found in bronchiectasis, where the pattern of the disease may be completely outlined and the feasibility of surgery determined. It is rarely employed in lung abscess, tumors of the lung or pulmonary tuberculosis. It should never be used routinely as a method of studying an unselected group of patients with thoracic disease.

Many methods of injection have been elaborated. Catheterization of the trachea through the cocainized larynx seems to afford the most precise control of the distribution of oil and the best control of the position of the patient for accompanying roentgen-ray studies. For detailed problems a special catheter may be inserted into individual bronchial segments and a record made by spot films under fluoroscopic guidance (Thompson; Goldman and Adams).

Bronchography by the injection of oil with the bronchoscope in place tends to give disappointing results. If it seems necessary to combine the two procedures, injection of oil should be done after the bronchoscope is withdrawn and the cough reflex has subsided.

The roentgenographic technic of bronchography must be systematic and thorough. A unilateral injection is first made and recorded by anteroposterior and lateral films. Following injection of the sec-

ond side, anteroposterior and oblique films are required. A great majority of the records made by those unexperienced in the procedure are worthless, as they yield only incomplete evidence and require repetition in the hands of an expert team.

BRONCHOSCOPY

The bronchoscope is as important in the diagnosis of chest disease as the proctoscope is in the study of the large bowel and rectum. In expert hands it is usually no more disturbing to the patient. In interpreting the findings of a bronchoscopy, however, the instrument's range of vision must be kept clearly in mind. This is limited essentially to the orifices of the first subdivisions of the lobar bronchi. With the aid of the fluoroscopic table foreign bodies may be recovered from more remote regions of the lung. The aspirating cannula may be inserted into the fine subdivisions. Visualization of pathologic lesions, however, and precise biopsies are possible only in the limited area designated.

Precision in the use of the bronchoscope is furthered by a complete preliminary study of the case. Exploratory bronchoscopy should be as unusual an event as exploratory laparotomy. Adequate fluoroscopic and roentgen-ray study usually results in requesting the bronchoscopist "to take a biopsy from the mass presenting in the first dorsal division of the left lower lobe bronchus" rather than merely asking him what he can see.

Barring the extraction of foreign bodies, the therapeutic potentialities of the bronchoscope are not so impressive as is its value in diagnosis. Its efficacy in the treatment of acute lung abscess is still questioned outside Philadelphia. The results in bronchiectasis are palliative, and only occasionally better than those attained with postural drainage. As an intensive preoperative measure the procedure may be helpful in building up the general condition of the patient. Small benign tumors may be removed successfully by the bronchoscopist, and areas of lung drowned in retained bronchial secretions drained by removing the obstruction due to larger tumors. Cicatricial stenosis may be dilated in some cases, with relief of symptoms.

The significance of a negative bronchoscopy in primary carcinoma of the lung depends entirely on the location of the tumor. Failure to obtain a positive biopsy when obstruction to a lobar bronchus has been demonstrated by x-ray is important evidence against carcinoma. Failure to reach a peripheral tumor is to be expected, and in fact, under these circumstances, bronchoscopy may not be advised.

The location of an area of suppuration may be designated by observing pus exuding from a bronchial orifice. The source of a positive tuberculous sputum may be determined if aspirated secretion from one lung is constantly negative and that from the opposite lung positive.

The clinical importance of tracheobronchial lesions has led to a more frequent use of the bronchoscope in tuberculosis. The ulcerative and stenosing lesions of this complication have an important bearing on the results of and the indications for collapse therapy.

EMPYEMA

During the influenza epidemic of 1918, high-pressure publicity was given to the intercostal-catheter method of drainage for acute empyema. In succeeding years the method was modified and amplified by an untold number of devices for the maintenance of negative pressure and the flow of irrigating solutions. As more emphasis has been placed on the principles of the treatment of empyema rather than on the details (Heuer, Graham), the enthusiasm for the rediscovery of complicated methods has calmed down.

The catheter method of intercostal drainage is a lifesaving measure under certain circumstances; it is also a very effective form of treatment for a large number of cases in infancy and childhood. In general, however, it is more difficult to carry out and leads to more complications in inexpert hands than does needle aspiration, followed by rib resection when the pus has thickened. The important principle to bear in mind is not to create a pneumothorax by any method in a patient who has a reduced respiratory reserve. Early in the 1918 influenza epidemic this was done by resecting a rib during the acute phase of streptococcal bronchopneumonia, and disaster naturally followed.

In the community at large there seems to be more difficulty arising from taking out the drainage tubes prematurely than from putting them in. In this regard it is emphasized that a tube should not be removed until the cavity has become obliterated. The most effective calibration of an empyema cavity is made by the injection of Lipiodol under fluoroscopic guidance.

Specific immunological measures may well lessen the incidence of empyema both in streptococcal and pneumococcal infections. There are already encouraging signs pointing in this direction.

LUNG ABSCESS

Putrid lung abscess remains one of the most destructive forms of thoracic disease and one of the most difficult therapeutic problems. A wave of animal experimentation seeking to throw light

on the pathogenesis of the disease swept over the country a few years ago. This has now subsided, leaving the conclusion that abscesses can be produced either by infected vascular emboli or by infection via the bronchial route. The majority of clinicians hold to the aspiration theory.

Because of the fact that approximately 20 per cent of all cases may be expected to heal spontaneously, there is still a tendency to prolong the period of expectant treatment to an illogical degree. Neuhof has recently been a strenuous advocate of "early operation." As a warning against dangerous delay his advice is sound. It has long been known that spontaneous healing rarely occurs unless definite signs of regression are observed during the first six weeks. Many surgeons still believe that at least this period should elapse in a majority of cases before operation is performed. This pause serves not only to allow spontaneous healing to take place but to permit subsidence of the concomitant pneumonitis. It is not clear from Neuhof's writings whether operation at the end of six weeks falls within his definition of "early."

Neuhof has also urged operation in one stage. The safety of this procedure is questioned by a number of surgeons experienced in the field, and he stands almost alone in making this recommendation. Aside from the dangers of contaminating the pleural space, a great deal is gained by the protection against infection of the chest wall which is afforded by the two-stage procedure.

Drainage of an abscess by no means ends the story in many cases. Sequestration of the lung commonly results in a defect that resists the processes of natural healing. In a few borderline cases the defect may be closed by turning a pedicle muscle graft into the cavity. The healing of residual apical cavities may be aided by thoracoplasty. It is becoming increasingly clear that the large defects must be treated by lobectomy or pneumonectomy if permanent healing is to be expected.

Certain cases of lung abscess in the subacute or chronic stage (two months and longer) present indications for primary lobectomy. A consideration of this method is particularly recommended in abscesses of the upper lobe, as they are notoriously difficult to drain adequately and are resistant in healing.

The Philadelphia group continues to report favorable results in the treatment of lung abscess by bronchoscopic aspiration. Success appears to depend on instituting treatment very early after onset. If improvement is not soon manifest or if the abscess recurs after a remission, recourse is had to surgical drainage.

A good deal of the confusion that exists regarding the therapy of lung abscess may be traced to variations in the clinical material of various institutions. An enthusiastic report (Nammack and Tiber) regarding the efficacy of guaiacol recently emanated from Bellevue Hospital. Careful study of the individual case reports shows that a predominant number of cases were what might be classified in other hospitals as septic pneumonitis from the aspiration of pharyngeal secretions or gastric contents during an alcoholic debauch. These cases are common in large municipal hospitals receiving admissions from the police ambulance service. Their clinical course is quite different from that of the putrid post-tonsillectomy abscess.

As a preventive measure, tonsillectomy and other operations in the nasopharyngeal region must be regarded as serious affairs, particularly in the adult patient. In elective procedures, oral hygienic measures should be undertaken as a preliminary step. Every effort should be made to minimize the extent of denuded areas that must heal by granulation attended by suppuration.

PULMONARY TUBERCULOSIS

The consultation services of a thoracic surgeon are now indispensable in any institution housing patients with pulmonary tuberculosis. Certain states (Connecticut and New York) have developed comprehensive programs that combine their several institutions in a unified surgical service. In Massachusetts the two state institutions are served by one consultant, and the eight county sanatoriums by at least four other consultants experienced in chest surgery.

Extrapleural thoracoplasty has become increasingly effective as the technic of its performance has been perfected. The principle of extrafascial apicolysis introduced by Semb, of Oslo, has been accepted in most clinics and is used as a routine adjunct to the removal of ribs. This procedure drops the apex of the pleura to the level of the fifth rib. Combined with the resection of long segments of the upper ribs, extrafascial apicolysis is so effective that thoracoplasty for upper lobe disease is rarely carried below the seventh rib.

A revival of extrapleural pneumothorax is well on its way. When intrapleural pneumothorax is impossible because of adhesions, the parietal pleura may be stripped from the chest wall and the space so created maintained by refills of air. It seems wise at the present to reserve this procedure for use in patients in whom thoracoplasty is certainly contraindicated. While very ill patients withstand the operation surprisingly well, it should not be considered a substitute for thoracoplasty on the grounds that it is a less disturbing procedure. In many cases thoracoplasty to close the space will

have to be performed at a later date, and when the mortality of late complications is included, it may be safely predicted that the risk of the procedure will be found greatly to exceed that of thoracoplasty. There are certain cases, however, in which it is being carried out as the only possible effective measure.

Phrenic nerve surgery has suffered a recession in popularity, at least east of the Hudson River. Permanent paralysis of the nerve is rarely performed, and temporary paralysis is carried out with far less frequency than a few years ago. The procedure has been found to be relatively ineffective, and what is more important, actually to increase the risk of a subsequent thoracoplasty. There are still distinct indications, however, for its use in carefully selected cases.

Bilateral thoracoplasty has on the whole been found disappointing. The removal of sufficient ribs to arrest the disease effectively is apt to leave the patient a respiratory cripple.

The goal of collapse therapy is a negative sputum, and laboratories have met this challenge by refinements in sputum examination extending through concentration methods to cultures and guinea-pig inoculations. Examination of the gastric contents is the final step when the patient no longer raises sputum. While these efforts are laudable and increase the understanding of the disease, it is difficult at the moment to know what they mean from a practical prognostic standpoint. Certainly many cases formerly classified as arrested by any form of treatment would now be found to be carriers of the tubercle bacillus.

BRONCHIECTASIS

Extirpation of the diseased areas of lung has long been the goal of those familiar with the pathology of bronchiectasis. Early efforts in lobectomy were attended with an operative mortality rate that was prohibitive. Attempts were then made to find a substitute, and collapse therapy by pneumothorax or thoracoplasty (Hedblom), cautery pneumonectomy (Graham), and exteriorization lobectomy (Whittemore) had their day. In 1926, Brunn revived the direct surgical attack. Shortly thereafter Shenstone devised the ingenious snare tourniquet that simplified the technical problems of dealing with the hilar stump. The development of bronchography made it possible to outline the pattern of the disease so that a systematic surgical program could be planned. The net result of these and other aids to diagnosis and technics has been a reduction in the operative risk of lobectomy from 50 per cent to less than 5 per cent. Surgery is now routinely recommended even in the milder cases of the disease.

An area of lung which is the site of established bronchiectasis must be regarded as irreparably damaged. No evidence exists that the pathologic lesion is a reversible one. The symptoms are notoriously variable in the same individual at different seasons of the year or at different periods in the course of the disease. In general, the initial insult to the lung structure occurs early in life and is of varied origin. The basic element in the pathology is a destruction of the ability of an area of the bronchial tree to rid itself of the secretions of the mucous membrane. The dilatations may remain "dry" and cause no symptoms for periods of years. Sooner or later, however, infection occurs and cough and sputum manifest themselves. Infection, favored by stagnation, leads to the characteristic odor from decomposing secretions. Hemorrhages result from ulcerations of the bronchial mucosa, and are infrequent when long-standing infection has erected a barrier of peribronchial fibrous tissue. In fact, hemoptysis is more apt to occur in the "dry" phase of the disease.

Established infection increases the tendency toward stagnation of secretions by hypertrophic changes of the mucous membrane. Acute episodes of pneumonitis spreading from the focus of the disease recur with increasing frequency. Pleurisy and empyema appear as complications. The accessory nasal sinuses quite commonly become infected and serve as an additional focus for the perpetuation of an endless series of respiratory tract infections, particularly during the winter months.

The progressive course of the symptoms has led to the conception that bronchiectasis is a progressive infection of the lung. As a matter of fact, the anatomic pattern of the disease is usually complete at the time the diagnosis is first made. Patients may progress to advanced stages of the disease with the production of a copious volume of malodorous sputum and still show a sharply localized lesion in one lobe or even a single portion of a lobe. Involvement of other areas of lung does occur, but usually as the result of an episode of acute infection. Other areas of lung become damaged by fibrosis and emphysema as a sequel to focal areas of pneumonitis or bronchitis.

A concept of the underlying pathology of the disease is essential to an understanding of its treatment. Conservative measures such as postural drainage, bronchoscopic drainage, local treatment of nasal sinusitis, vaccines, change of climate and sanatorium regimen may be classified as symptomatic treatment. Certain of these measures are to be employed when contraindication to operation is present, or may be useful to prepare the patient for operation. Curative treatment resides only in surgical extirpation of the diseased area of lung.

Certain bilateral cases have been made the sub-

jects of bilateral lobectomy. These cases require careful selection and accurate appraisal of the lung tissue that is to remain. They will always constitute a small group so far as surgery is concerned.

While the ideal case for operation presents a localization of the disease to a single lobe, technical methods are being developed to deal with foci of bronchiectasis scattered throughout several lobes. In cases coming to operation before the dense scarring of chronic infection offers a barrier, segmental resection of diseased areas with conservation of normal lung substance may be possible (Churchill).

Cases of bronchiectasis or cystic disease involving an entire lung may be cured by total pneumonectomy. In the presence of active infection this becomes one of the most formidable operations of thoracic surgery and carries a correspondingly high risk, approximately 35 per cent. The chief hazard lies in uncontrolled hemorrhage from the vascular adhesions that fuse the lung with the chest wall. A second hazard lies in the postoperative infection of the pleural space, mediastinum and chest wall. Amputation of the hilus usually requires use of the tourniquet technic rather than individual ligation of the vessels as in primary carcinoma.

The appraisal of the possibilities of surgery in bronchiectasis centers about a precisely done and complete bronchogram. Disappointing results will follow a failure to delineate completely the pattern of the disease before embarking on a surgical program.

PRIMARY TUMORS OF THE LUNG

The most outstanding achievement in the field of chest disease during the past decade has been the extension of knowledge concerning primary tumors of the lung. Internists, radiologists, surgeons and pathologists have found the subject a productive field for their best efforts, and the accumulated literature has assumed vast proportions.

The most spectacular operation of thoracic surgery — total pneumonectomy — has emerged as the answer of the surgeon to the challenge of hopeless malignant disease. It is now a little more than five years since the first successful removal of an entire lung for epidermoid carcinoma (Graham). Although the vast majority of cases reach the surgeon at a time when the possibility of arresting the disease by extirpation has passed, sufficient experience has been accumulated to demonstrate the feasibility of the procedure from a technical standpoint.

The operative risk of total pneumonectomy is high. Statistics dealing with operative mortality are at the present time so colored by variations in the criteria of operability, as well as variations in the technics employed, that an estimate, if given conservatively, is of more significance than a thorough analysis of reported cases. As a conservative estimate, it may be stated that the hospital mortality for total pneumonectomy in the absence of a preoperative element of infection is leveling off at about 20 per cent; with infection, at between 35 and 50 per cent.

Statistical evidence regarding the frequency with which the surgeon is able to arrest carcinoma of the lung will not be available for many years. Certainly there is no reason to believe that surgery will be more or less efficacious in dealing with pulmonary carcinoma than it has been, it might be said, with carcinoma of the stomach. While enthusiasm is being centered about patients surviving the operation, it must not be forgotten that the operation is being undertaken for cancer.

Total pneumonectomy may be carried out by individual ligation of the vessels and careful suture of the main bronchus unless an inflammatory barrier makes dissection within the mediastinum impossible. In the latter event, tourniquet amputation becomes necessary. In the absence of gross contamination from an infected lung (pneumonitis, obstructive endobronchial suppuration and even actual abscess formation are frequent concomitants of pulmonary neoplasms), the pleural cavity may be closed without drainage and healing by first intention secured. If infection of the pleural space ensues, drainage is employed and a thoracoplasty to obliterate the unilateral empyema cavity performed at a later date.

The pendulum has swung to the extreme point of view in regard to total pneumonectomy as the only operation for primary carcinoma of the lung. It is the ideal operation in the sense that it offers a more complete eradication of the primary growth and adjacent lymph nodes than any more limited procedure. It will be required in a majority of cases by reason of the anatomic site of the primary growth. It is not the ideal operation, however, if patients without lymph-node involvement are going to be sacrificed because of the high operative risk that it entails. The prospects of cure of any cancer are relatively so poor, once regional metastases have taken place, that an effort routinely to extirpate regional lymph nodes at a high price in operative mortality seems of doubtful wisdom. For this reason, lobectomy, if the primary growth and any demonstrably involved lymph nodes can be removed thereby, should still find a place in the treatment of lung tumors.

A positive preoperative diagnosis materially

strengthens the hand of the surgeon in assuming such a serious responsibility. This may be obtained by bronchoscopic biopsy in approximately 70 per cent of all cases, but in a smaller percentage of the operable group. The latter will include a relatively large number of peripheral tumors that cannot be reached with the bronchoscope. In many cases, therefore, operation must be advised and carried out in the absence of a preliminary microscopic diagnosis. Expert roentgen-ray technic and interpretation is essential under these circumstances.

A primary tumor arising in the bronchial wall and superficially resembling bronchogenic carcinoma has been variously referred to as "benign adenoma" or "carcinoid." Whatever the histogenesis and nature of this tumor are ultimately proved to be, clinically and prognostically it differs sharply from carcinoma. Invasion is extremely slow and limited in extent, and metastasis is extraordinarily rare. Many such tumors, however, require radical extirpation because of the damage done to the lung by long-standing bronchial obstruction and infection.

Unfortunately, these tumors are still being confused with cancer, and inclusion of them in end-result studies gives a distorted picture of both operative mortality and ultimate survival. These tumors are observed with a frequency of 1 to 10 true carcinomas. Of the group of resectable bronchogenic tumors, however, they comprise 25 per cent in the Massachusetts General Hospital series (8 adenomas to 24 resectable primary bronchogenic carcinomas).

Whether or not this tumor is potentially malignant, its inclusion in statistics purporting to deal with cancer will give rise to undue optimism in the interpretation of results. If for no other reason, the adoption of the classification suggested by Womack and Graham must be accepted with caution.

HEART AND GREAT VESSELS

The most spectacular achievement of the decade in the surgery of the heart and great vessels has been the successful closure of a patent ductus arteriosus in 4 cases by Gross. Without detracting from the brilliant achievement of the surgeon, our compliments must be extended to the internist, Hubbard, who had courage to recommend the operation to his patient. Many of the "firsts" in surgery await the conjunction of an internist with imagination, a surgeon with courage and skill and, last but not least, a willing patient.

Attempts to provide an artificially produced collateral circulation to the myocardium in cases of insufficient coronary circulation have been made by Beck in this country and O'Shaughnessy in London. Beck has utilized the muscles of the anterior chest wall, and O'Shaughnessy the omentum fixed in contact with the surface of the heart. Painstaking experimental observations on animals have served as a basis for the clinical experiment. Encouraging results are claimed by both workers.

Successful suture of wounds of the heart is now commonplace in the South. Elkin of Atlanta and Bigger of Richmond have materially added to the clinical diagnosis and operative technics of cardiac suture.

Decortication of the heart for constrictive pericarditis (Pick's disease) has become firmly established as a therapeutic procedure. Additional light on the disturbed mechanics of the circulation has been provided by the observations of Burwell and his co-workers on cardiac output before and after operation. White believes that the syndrome is rarely if ever of rheumatic origin. Tuberculosis seems the most probable etiology in a majority of cases but can rarely be proved by direct evidence.

ESOPHAGUS

The time is ripe for a more determined surgical attack on carcinoma of the esophagus. Irradiation has been shown to destroy the tumor in certain cases, but leaves a legacy of fibrosis which perpetuates the obstruction. Sporadic success with surgical extirpation has been reported over a period of years, but many technical problems require a more extensive experience for their solution. In an early case surgery should be considered the procedure of choice.

Perforation of the cervical esophagus has been labeled a surgical emergency by Pearse. He recommends immediate exteriorization of the perforation by a cervical incision and packing. Mediastinotomy, he says, may be advisable in perforations below the fourth thoracic vertebra.

A controversy still rages between the proponents of a two-stage and a single-stage operation for the common pharyngeal or pulsion diverticulum. Lahey favors the two-stage procedure, whereas Shallow reports a large series of cases done by the single-stage method. There is no generally accepted answer at present.

MEDIASTINUM

The mediastinum has established a reputation as the domicile of large rounded tumors which stimulate a guessing game in preoperative diagnosis. In general, the neurogenic tumors, neurofibroma and ganglioneuroma, tend to be situated posteriorly, and the teratomas and dermoid cysts anteriorly.

Intensive irradiation of these tumors in the absence of a definite diagnosis is to be heartily condemned. In certain cases it may be advisable to give a "lymphoma" dosage as a diagnostic measure. If the tumor regresses it is obviously not one that should be treated surgically; if it does not respond to light irradiation, surgical exploration to determine its nature and remove it if possible is indicated. Excellent results are obtainable in the group of benign tumors and cysts.

DIAPHRAGM

The thoracic approach is commonly recommended for the repair of rupture of the diaphragm — a not infrequent result of severe trauma. Rupture of the diaphragm with displacement of abdominal viscera into the pleural cavity is to be differentiated from hernia through an anatomic hiatus. Hernia through the esophageal hiatus is observed quite commonly by radiologists, but only rarely can be fixed on as the cause of symptoms. This lesion may be repaired by the abdominal approach. Harrington has presented a carefully considered anatomic repair of this defect and cites his experience with a large series of cases. Surgical repair of eventration of the diaphragm has not been reported, and presents a difficult problem.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25241

PRESENTATION OF CASE

First Admission. A sixteen-year-old girl was admitted complaining of pain in the right knee.

For the past four months she had had a dull aching pain in the right knee made worse on walking. During the last two months she had been unable to flex or extend completely the knee. There was no pain at night if she lay on her back holding the right knee sideways; lying on her face caused pain. The knee gradually became swollen, more so at night. The pain and swelling slowly became worse, and one month before admission it became constant. During the previous two months the right ankle became slightly swollen and painful at night. There was no history of injury, locking, inflammation, fever, night sweats or pain elsewhere. Her past and family histories were noncontributory.

Physical examination showed a well-developed and nourished girl in no acute distress. Examination of the heart revealed a loud blowing systolic murmur loudest over the pulmonary area. The blood pressure was 140 systolic, 85 diastolic. The patient walked with a limp, holding the right knee at about 20° of flexion. The right knee was somewhat swollen, and the right leg above the knee was slightly wasted. Moderate tenderness was present over a somewhat firm swelling along the anterior edge of the tibia just below the patella.

The temperature was 98.6°F., the pulse 80, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 5,000,000 with 80 per cent hemoglobin, and a white-cell count of 14,400 with 68 per cent polymorphonuclears. A blood Hinton test was negative. Tuberculin tests in dilutions of 1:5000 and 1:1000 were negative. The blood serum calcium was 10.93 mg. per 100 cc., the phosphorus 4.64 mg., and the phosphatase 2.86 Bodansky units.

X-ray films showed a large area of diminished density involving the central portion of the head of the right tibia. There was marked thinning of the cortex, the process extending to the articular cartilage. The area was trabeculated. The lower border was somewhat irregular. There was very little evidence of expansion, the cortex being intact. The lower femur showed some diminished radiance probably due to atrophy. Films of numerous other bones showed no evidence of disease. The chest was negative.

On the eighth hospital day operation showed a typical giant-cell tumor which was shelled out, and the cavity curetted. The upper end of the normal shaft of the tibia was then chiseled obliquely and the cavity filled with periosteum and soft parts. A tongue-shaped flap of periosteum was allowed to drop back into the cavity. The pathological report on the tumor was benign giant-cell tumor. The patient rapidly recovered and was discharged on the twenty-ninth hospital day.

Second Admission (four years later). Following discharge the patient remained perfectly well until eight weeks before re-admission when, without trauma or other known exciting cause, she began having dull intermittent pain in and just below the right knee. It gradually became more or less continuous, especially at night. Three or four weeks before entry the pain became so severe that she was forced to give up her work in a shoe factory. She began using a cane. The knee then began to assume a permanently flexed position. Swelling then occurred in the region of the old operative incision and increased until it involved the entire lower leg when the leg was kept in a dependent position. The pain then became quite localized to the area beneath the operative incision. The appearance of the skin did not change. During the previous two weeks she had used crutches. There was no pain elsewhere, and no fever or malaise. She had lost about five pounds in weight in the past three months.

Physical examination was negative except for the right leg. Over the medial aspect of the proximal end of the right tibia there was a dome-shaped mass 7 cm. in diameter and 2 to 3 cm. high, which felt tense and slightly fluctuant in its midportion. There was a healed scar overlying it. It was apparently fixed to the underlying structures and to the tibia. The skin surface was possibly slightly warmer than that of the opposite leg. The mass was slightly tender throughout, but especially so in the anterior portion. There was no evidence of increased fluid in the joint. The inguinal lymph nodes were not enlarged. The right calf and thigh showed evidence of atrophy.

The temperature was 97.8°F., the pulse 88, and the respirations 20.

The urine examination was negative. The blood showed a red-cell count of 5,600,000, and a white-cell count of 10,720 with 84 per cent polymorphonuclears. A blood Hinton test was negative. The serum calcium was 10.77 mg. per 100 cc., the phosphorus 3.6 mg., and the phosphatase 4.24 units.

X-ray films showed an area of diminished density in the extreme upper end of the right tibia with rather ill-defined margins and measuring 4 cm. in diameter. In the central portion of this area the trabeculae were increased in density and were rather mottled in appearance. The bone surrounding the area was dense and sclerotic. There had been a considerable amount of new-bone formation in the operative area medially. There was slight tilting of the joint surface of the tibia toward the medial side.

On the fourth hospital day an operation was performed.

Differential Diagnosis

Dr. Charles C. Lund:* This is the type of case where the x-ray is of special importance in making a diagnosis. I wonder if we could see the films now.

Dr. Tracy B. Mallory: The x-rays on the first admission are not available. They have been sent to the Bone Registry, but no one who has seen them questions the statement that the picture is entirely typical of a benign giant-cell tumor. Dr. Schatzki will show you the subsequent films.

Dr. Richard Schatzki: The first film is a postoperative film and shows the location of the lesion and the postoperative defect.

Dr. Lund: At the first admission?

Dr. Schatzki: Yes, in 1934.

Dr. Lund: The triangular-shaped defect is at the upper end of the tibia on the medial side and measures about 5 by 5 by 5 cm. It leaves a lateral margin of the tibia that is a little bit wider than the fibula.

Dr. Schatzki: Four years later there is marked regeneration of bone in the area of operation. A cavity-like defect is seen in the midportion of the condyles of the tibia which apparently was present at operation and represents the area of the original tumor. The appearance of this cavity has, however, changed. There are small chip-like areas of new-bone formation in this region. The soft-tissue mass described in the report extends over the upper edge of the cavity along the medial aspect of the tibia and shows nothing but a homogeneous soft-tissue shadow.

Dr. Lund: Going now to the postoperative film there is complete removal of this triangular area of bone. Looking closely in connection with what has developed since, one sees that the epiphyseal region is denser than the area on the other side and does not look as though there had been complete removal of any process that may have been there. It looks to me as if there possibly had been only partial removal of diseased bone in that part; but of course I cannot be sure of that. In the recent film one sees filling in this area of increased radiance, an irregular area of increased density, and in addition a definite soft-part tumor medially, with a little break in the somewhat irregular contour of the healed bone.

In the early part of this century, I think probably largely due to some of Dr. E. A. Codman's work, a clear distinction between the various primary tumors of the bone began to be made and people started to realize what had not been appreciated in the latter part of the last century, namely, that the group of bone tumors with foreign-body giant cells scattered through the tumor tissue were not in any way like the osteogenic type of tumor. A great many amputations had been done in the past for cases that were not very malignant. When I was a student and intern — which is now going on to twenty years ago — we were taught that the giant-cell tumor was not malignant. But shortly after that, due to further work by Dr. Codman and particularly presented in a paper by Dr. Simmons,[1] that was shown to be untrue. There are cases of giant-cell tumor that without changing their pathologic character have the ability to metastasize and there are cases of apparently very definite giant-cell tumor that shift over into what may be called osteogenic tumors. With that background we have to consider whether in this case the process that was present on reentry was a recurrence of a giant-cell tumor, whether it was a development of an osteogenic type of tumor in the presence of what was originally a giant-cell tumor, or whether it was something else entirely different. This soft-part tumor bothers me a great deal because I should not expect a mass of that size with no calcification in connection with either of the two types of process that I have just described. Moreover this was described as a semi-fluctuant mass, which makes one think of infection. There is no other evidence pointing in that direction, however. The temperature was not raised, and the white-blood-cell count not elevated, and a remote infection at this late date, four years after operation, can be quite well ruled out. Finally, I think it would be unreasonable to consider here any process totally unconnected with the original one, such as metastatic malignancy or a new disease.

Just a word more and then I shall make an attempt at a diagnosis. Of course the clinical diagnosis here is highly unimportant. This is one of the cases where the surgeon rightly puts all the responsibility on the pathologist. One should not decide on the x-ray and clinical evidence what type of surgery was indicated. All one should decide is that a biopsy was indicated, and

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then following the opinion of the pathologist one should be ready to go ahead with some kind of surgery, either a local removal or an amputation. It would be very difficult to plan any local removal of this process that would result in a useful leg. One might think of x-ray treatment, but such a decision depends on the diagnosis. There is one other bit of evidence to be considered — the chemical data. If she had a high blood phosphatase one would think that the tumor had probably shifted to an osteogenic type of malignancy in place of the giant-cell tumor. This particular phosphatase is not high enough to mean much.

For my first choice I am going to say that this process is a recurrent giant-cell tumor, and for my second choice, an unusual osteogenic sarcoma.

Dr. Ernest A. Codman: This case was of unusual interest to me, not only because the patient was a very brave girl, but because there were a good many features in the case that were very instructive. Dr. Lund, calling attention to the x-ray taken after the operation, assumed that the removal of the tumor had been incomplete. The fact is that the whole tumor was shelled out from beneath the joint cartilage and from the bony walls of the head of the tibia. Moreover the inner walls were smooth, and there was no gross evidence of invasion by the tumor. Dr. Lund was deceived by this film because the posterior wall of the cavity remains intact, but the tumor was completely removed and a wedge-shaped flap of periosteum turned into the cavity with the express idea of having it develop on the line of stress according to Wolff's law, to form new structural bone. She did obtain good use of the leg; many of you saw her two years ago at the meeting we had on giant-cell tumors. She had perfect function and almost perfect contour for four years. Then suddenly, in November, 1938, acute pain began and was soon followed by swelling. She had had good function for four years. When she entered the hospital, the tumor was fluctuant, so that I hoped that it was an abscess, due possibly to a sequestrum, but when I explored I found a very malignant almost purely cellular tumor with no giant cells in it; it was quite different histologically from the original one. There were many mitoses.

She refused amputation at first but two weeks later we persuaded her to have it done, and Dr. Van Gorder removed the leg. She went home and almost immediately developed metastases in the lungs and died. The duration from the development of signs of recurrence to death was only four months, and yet for four years after operation there had been no trouble.

To me one of the most interesting facts to record is that at this operation I made the incision in the bone well below the tumor for the express purpose of finding what we call a concavoconvex line in the marrow. A giant-cell tumor always has a visible sharp concavoconvex line separating the marrow from the tumor tissue. In cases of osteogenic sarcoma there is always an irregular extension up into the medulla above the obvious tumor; that is, the tumor extends up in the medulla higher than the x-ray shows it. In giant-cell tumors, the x-ray shows this concavoconvex line. I made my periosteal flap starting about 5 cm. below the tumor and took away the cortex in order to look at this line to see whether it was typical of giant-cell tumor. In the past I have taken every opportunity I could to examine the medullary invasion in different forms of tumor at the medical school museum and in registered cases. I find it almost an invariable rule that the concavoconvex line is present in giant-cell tumor. In the paper I wrote about this case[2] I made the statement that I believed that the surgeon should decide for himself, on finding that line, that it is one of a giant-cell tumor and go ahead and treat it as such. That line was present in this case and was perfectly typical.

Then another point, the gross appearance was characteristic. The surgeon knows the "currant jelly" appearance of this kind of tumor. Moreover, another gross sign was present. It shelled out easily, as it always does in giant-cell tumors, and very little was left on the edges or on the clean wall inside. Still another point in the gross appearance was its extension to and limitation by the joint cartilage. Of course the x-ray film is a little deceptive because the posterior wall was still present, but the whole thing was cleaned out. There were, however, little irregularities in the smooth walls where cells might have stayed. I purposely did not use a chemical cautery to remove such cells as might have been there, because I felt that they were probably giant-cell tumor cells and were of little danger.

Now, could such a malignant type of cell as we found at the second operation have been there for four years, together with the gradually developing new bone? The patient walked around perfectly freely without pain. If it was a malignant tumor in the beginning it took a long time to recur. Its rapid growth, when it appeared the second time, suggests a new tumor. This case was registered and went the rounds; all the men on the registry committee wrote "giant-cell tumor" on the specimens — as I think they would today. I believe that this is a very critical case in showing that surgeons and pathologists together cannot tell a giant-cell tumor every time. Dr. Simmons several years ago pointed out that 7.5

per cent of supposed giant-cell tumors later developed into real malignant tumors. Recently when I went over the tumors of the knee joint I found almost exactly the same percentage. I think this is a minimum rather than a maximum figure, because I have found so many cases, in this community, where supposed giant-cell tumors later showed malignant changes. For instance, there was a case at this hospital which Dr. S. M. Roberts operated on and filled with bone chips. Dr. A. R. MacAusland, Dr. R. B. Osgood, Dr. C. C. Simmons, Dr. F. J. Cotton and others have had such cases. This case is especially important because it was so carefully studied by men as well qualified to know a giant-cell tumor as anybody. I personally took the responsibility of not using postoperative x-ray treatment. I am not sure now whether such treatment should be advised as a routine; of course several of the other cases that had malignant changes recurred in spite of postoperative x-ray therapy. We have also had cases in which x-ray treatment alone was used but in which the same result occurred.

Dr. Channing C. Simmons: I have very little to add to what Dr. Codman has already said. There are three possibilities. First, there is a type of central fibrous osteogenic sarcoma that is often confused with a giant-cell tumor because it contains a few foreign-body giant cells. These are central tumors with bone destruction which in the radiogram does not extend to the epiphyseal line, otherwise the films closely resemble those of giant-cell tumor. Microscopically, foreign-body giant cells are found in the periphery of the growth. There have been four cases of that character in the hospital. Secondly, I believe the pathologist cannot always tell whether a given giant-cell tumor is malignant or benign. Thirdly, I believe a great many of these cases are benign giant-cell tumors primarily, but as the process of repair goes on and there is an attempt to fill the cavity with normal bone, the mesoblastic tissue making this repair finally takes on malignant characteristics and becomes an osteogenic sarcoma. I believe that this patient had a benign giant-cell tumor in the first place, and as a result of the process of repair, she developed an osteogenic sarcoma. At the present time I think it is difficult to distinguish between the two latter groups.

Clinical Diagnosis

Recurrent giant-cell tumor.

Dr. Lund's Diagnosis

Recurrent giant-cell tumor.

Anatomical Diagnosis

Osteogenic sarcoma.

Pathological Discussion

Dr. Tracy B. Mallory: I agree with Dr. Simmons. I find it difficult to believe that a mistake could have been made on the original tumor because both x-ray and histological findings were so perfectly typical of a benign giant-cell tumor. Benign giant-cell tumors can of course recur but usually in a much shorter period than four years. It would seem more reasonable to me to accept the simple explanation that Dr. Simmons gave; namely, that in the process of repair a true malignant osteogenic sarcoma developed.

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CASE 25242

Presentation of Case

First Admission. A forty-four-year-old white married woman was admitted complaining of pain in the left lower quadrant of the abdomen.

The pain first appeared about eight months before admission as a dull aching sensation in the left side of the lower abdomen an hour after eating. It occurred once a week and lasted from one to three hours. There were no other gastrointestinal disturbances. No medicinal or mechanical relief could be obtained. It seemed to be especially related to the eating of gas-producing foods. During the previous two months the pain had increased in intensity. Three weeks before entry the ache became unrelated to eating and was present when she assumed a sitting position. Bending forward caused increased pain, whereas standing gave partial relief. The pain had remained in the same position. She noticed tenderness in the left abdomen to her own palpation. The ache was noted every day until entry, lasted most of the day, and disappeared at night. It had never been sharp, had never radiated and was unrelated to respiration. During the previous two months there had been slight nausea in the morning, but she had never vomited, except on one occasion two weeks before entry after eating some fish which she ordinarily did not tolerate. During the previous two months she had had a diurnal frequency of five times and nocturia four times.

Her uterus had been removed two years previously for fibroids. She had severe headaches about once a month which lasted about six hours and seemed to be related to menstruation. She also had painful hemorrhoids. For the past six months she had had occasional hot flashes and

spells of weeping. Her past and family histories were otherwise noncontributory.

Physical examination showed a well-developed and nourished woman in no acute distress. Examination of the chest was negative. The blood pressure was 135 systolic, 74 diastolic. Deep palpation of the left abdomen beneath the costal margin gave the impression of a mass descending with inspiration. Pelvic examination revealed a moderately relaxed pelvic floor. Rectal examination showed a number of tender protruding hemorrhoids.

Examination of the urine was negative. Examination of the blood showed a red-cell count of 4,800,000 with 90 per cent hemoglobin, and a white-cell count of 8200 with 51 per cent polymorphonuclears. A blood Hinton test was negative.

X-ray films of the abdomen showed that the left kidney was obscured over its lower pole by a soft-tissue shadow which also partially obscured the psoas muscle. A retrograde pyelogram showed that the upper calices of the right kidney were deformed and pushed downward. The left kidney pelvis was large but not deformed. The ureters were normal.

The patient was kept in the hospital for nine days, but no obvious cause could be found for her complaints. The hemorrhoids were removed. She was discharged with a diagnosis of psychoneurosis, menopause, relaxed pelvic floor and fissure in ano.

Second Admission (seven years later). Two years before the second admission the patient entered the Out Patient Department, at which time two blood Hinton tests were positive, two Wassermann tests negative. She gave no history suggestive of primary or secondary syphilitic infection, and her husband had had a negative blood Hinton test in this hospital. She had had one miscarriage, her first pregnancy, but had three other children living and well. Her oldest daughter had had sore eyes at the age of nine years and subsequently had some injections at an outside hospital. The patient had become moderately obese during the past few years and was coming to the Out Patient Department for diet control. Twenty-two months before entry she was said to be losing weight too rapidly, had headaches, was nauseated and was unable to retain food. Two months later she complained of pain in the left axillary region, but examination of this region was negative. She continued having severe headaches about once each month, with hot flashes, nausea and vomiting. Four months later the blood showed a positive Hinton test and a weakly positive Wassermann test. She was being given courses of bismuth and salvarsan treatment. One year before entry her youngest child, an eleven-year-old boy, entered the hospital with cirrhosis of the liver. His blood Hinton test was negative. X-ray films of the patient's chest ten months before admission were negative except for slight prominence of the left ventricle. Eight months before admission she had had a severe attack of upper abdominal pain occurring an hour after her evening meal, followed in two or three hours by severe vomiting and relieved by a hypodermic injection. Two months later she had had a similar attack. On each occasion the pain was gone the following day. Four days before admission, during the evening, there was a sudden onset of crampy, intermittent, severe upper abdominal pain, radiating to the back and to the right and left. Nausea and vomiting were associated with the pain so that she could retain nothing by mouth. The vomitus consisted of sour brownish material. During the day before admission she vomited almost continuously. She had had only one bowel movement during the four days. There had been no jaundice.

Physical examination showed a well-developed and nourished woman in obvious distress, complaining of abdominal pain. Examination of the chest was negative. The blood pressure was 120 systolic, 80 diastolic. The abdomen showed diffuse abdominal tenderness, without spasm but with slight distention and tympany. No fluid or masses could be made out. Pressure in the lower quadrants caused pain in the upper quadrants. Rectal examination showed tenderness on both sides. Pelvic examination was negative. The uterus was absent.

The temperature was 101°F., the pulse 110, and the respirations 20.

Examination of the urine was negative. The blood showed a white-cell count of 9000. The nonprotein nitrogen of the serum was 17 mg. per 100 cc., the chlorides 110.4 milliequivalents, and the van den Bergh 1.5 to 2 mg. A stool examination was guaiac negative.

A flat abdominal roentgenogram showed marked distention of the jejunal loops. There was little or no air in the lower small intestine and colon. A Graham test was positive.

On the third hospital day the patient had a chill followed by a temperature of 102°F. The chest was clear. She had no abdominal pain or tenderness. The skin was slightly icteric. Two days later she was doing well on a soft diet and had no pain, nausea or vomiting. Her chart was flat.

On the tenth hospital day an operation was performed.

Differential Diagnosis

Dr. Robert R. Linton: It appears to me as if this patient must have had something in her left upper abdomen on her first entry, although they did not include it on her discharge diagnosis. I also assume she had no further x-ray studies.

Dr. Aubrey O. Hampton: Not until 1934, two years later.

The right kidney deformity seems to be due to rotation from pressure of the liver. I do not believe there is a tumor of the kidney. The soft-tissue shadow described here is not very obvious.

Dr. Linton: The following points I believe are of significance: In a review of the first admission I am unable to make a definite diagnosis any more than the service was at that time. X-ray study showed that there was something in the left side of the abdomen and it seems a little odd that she did not have a gastrointestinal series and also a Graham test, if there was something pressing on the right kidney. It seems conceivable that it could have been a large gall bladder. It is not unusual in gall-bladder disease to have pain in the left side of the abdomen and even in the left lower quadrant. This is due to pancreatitis secondary to the gall-bladder disease.

"Her oldest daughter had had sore eyes at the age of nine years and subsequently had some injections at an outside hospital." That points toward a child with congenital syphilis. With these positive Wassermann tests we have to assume that the patient had a positive blood. Whether she had any other evidence of syphilis, I am not sure.

"One year before entry her youngest child, an eleven-year-old boy, entered this hospital with cirrhosis of the liver." That is a statement on which I should like a little more confirmation.

In summary I should say the diagnosis rests between two conditions. Are we dealing with gall-bladder disease with gallstones and pancreatitis or with partial intestinal obstruction? In reviewing her first admission the former diagnosis I should think is the one to favor. I shall rule out the kidneys as I see no further evidence that they were involved. The important thing is the question of gall-bladder disease and pancreatitis, and I do not think one can make a diagnosis of gall-bladder disease alone. Some other condition should be associated with it because of the fact that she had severe nausea and vomiting, and on account of the brownish character of the material she vomited. I have always remembered the teaching of Dr. Daniel F. Jones, that in simple gall-bladder disease patients very seldom, if ever, vomit to any degree, and that if they vomit large amounts and the vomitus is brownish in color, as in this case, one must look for some cause other than cholecystitis and gallstones. Certainly pancreatitis, if associated with it, would produce such a picture.

She made quite a rapid response to conservative treatment, as I judge she was in fairly normal condition when they operated on her. A point I cannot overlook, however, in making a final decision in diagnosis is the x-ray report which says a flat abdominal x-ray film showed marked distention of the jejunal loops. There was little or no air in the lower small intestine or colon. In addition it is of significance that she had had only one bowel movement in four days. May we see the x-ray films?

Dr. Hampton: The proximal loop of the jejunum is markedly dilated, and there is a very sudden stop in the upper abdomen with nothing to suggest dilated small bowel below the second loop of the jejunum. There are ten dense pills in this dilated loop, and if you knew when they were given, it might help a lot.

Dr. Linton: The fact that these pills were undissolved — I do not know what the pills are — rather points to the fact that they were being held up in the upper intestinal tract because of some obstructive lesion where you see the dilated loops of intestine. I think that this would also help explain the severe nausea and vomiting that she had prior to entry. It is a little surprising, however, that she got over this if she did have as complete obstruction as that would indicate. However, intestinal obstruction is sometimes intermittent due to a valve-like obstruction and the intestinal contents will pass along, especially if the obstructed loops are decompressed by nasal catheter drainage, until the upper loop becomes distended again.

I should say that there was no question that the cause of this patient's final admission to the hospital was intestinal obstruction involving the jejunum. The exact nature of the lesion I am afraid I cannot state. It was probably malignancy of some type. I do not believe it was a gallstone impacted in the jejunum, as gallstones, if they ulcerate through into the intestinal tract, are usually held up at the ileocecal valve. I have to make a diagnosis of cholecystitis, possibly cholelithiasis as well, but I think these are probably incidental. My final diagnosis is obstruction of the jejunum due to a malignant tumor, with a question of cholecystitis and cholelithiasis.

A Physician: What were the pills?

Dr. Hampton: They remind me of sodium chloride pills. There are ten, and I wonder if they were given all at once.

Dr. Fiorindo A. Simeone: They were pills containing mercury that she was taking for antisyphilitic treatment.

Dr. Hampton: At what intervals?

Dr. Simeone: She took several a day. She was not definite as to the number taken per day or at what intervals.

Dr. Hampton: Do you think they had been there for days?

Dr. Simeone: I think so. She did not remember when she took them.

At operation she had a negative gall bladder. The organ was thin walled, soft, not distended and compressed easily, and there was nothing palpable in the common duct. Exploration of the abdomen revealed a tumor in the jejunum. The tumor delivered into the wound very easily; it was in the antimesenteric wall of the jejunum and was shaped like the fundus of the uterus. It was firm to touch and had small nodules over the surface measuring 0.5 to 1 cm. across. The nature of the lesion was not clear at the time. It was resected and the continuity of the jejunum reestablished by side-to-side anastomosis.

Dr. Hampton: Did the bowel look as if it had been intussuscepted?

Dr. Simeone: No; but it looked as if there had been partial mechanical obstruction for some time. The proximal end was somewhat dilated and hypertrophied.

Preoperative Diagnosis

Cholelithiasis and chronic cholecystitis.

Dr. Linton's Diagnoses

Malignant tumor of jejunum, with partial intestinal obstruction.
Syphilis.
Cholecystitis and cholelithiasis?

Anatomical Diagnosis

Malignant lymphoma, giant follicular type, of jejunum.

Pathological Discussion

Dr. Tracy B. Mallory: There was a quite marked, firm infiltration of the walls of the bowel for some distance, and the lesion was obviously neoplastic in gross. We were considerably surprised, however, by the final microscopic findings since this turned out to be a lymphoma of the giant follicular type. We have seen that type of lymphoma in many locations before, but we have never seen it as an isolated tumor of the bowel. It is, of all forms of lymphoma, the most slowly growing and the most clinically benign, so I think it is within limits of probability that she had had this tumor throughout her history. It is a little interesting that the medical student who saw her on the first entry made a diagnosis of lymphoma, though he did not place it in quite the right spot.

In these lymphomas of the gastrointestinal tract surgical resection may be the best form of treatment. We have had a number of cases with very long remissions — running from three to seven or more years — following surgical resection, and I think there is every reason to look forward to a long period of remission in this patient, although there is also no doubt that the tumor will eventually recur in some other spot.

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THE ANNUAL MEETING

Under the auspices of the Worcester District Medical Society the City of Worcester opened wide its doors to welcome the Massachusetts Medical Society, June 6, 7 and 8, for the celebration of the one hundred and fifty-eighth annual meeting.

The new beautiful and commodious Municipal Memorial Auditorium provided ample space and accommodations for the section programs, scientific exhibits, motion pictures and commercial displays as well as for the Council meeting and that of the Society.

Registration was promptly underway at nine o'clock Tuesday, and practically all the exhibits were in order because of ample preconvention time, in contrast with the confusion and noise of former years. This better state of affairs justified the change of opening time from Monday to Tuesday.

There was an unfortunate delay in getting the Bancroft Hotel Ballroom ready for the Shattuck Lecture, but the large assemblage waited patiently until arrangements were completed, and Dr. Wilder Penfield must have been gratified with the close attention of the audience, which was treated to a scholarly and illuminating discussion of epilepsy and cerebral lesions of birth and infancy, with records of the results of treatment. This delay was no fault of the Committee of Arrangements.

The educational exhibits were of exceptional quality and were studied carefully by a large proportion of the fellows because of the variety and practical importance of the subjects presented. These, together with the motion pictures, made contributions to postgraduate education which were enthusiastically approved.

There were 1134 fellows and 257 ladies in attendance during the three days, making a total registration of 1391 thereby exceeding that of any previous annual meeting of the Society outside of Boston.

For the first time, the section meetings were carried through on a continuing program. As in previous years, the same was true of the combined meeting on Wednesday morning. This custom was generally approved. The only overlapping exercises were the round-table discussions on Wednesday afternoon.

Guest speakers from many important clinics brought the consensus of medical teaching to amplify the addresses of our members. The subjects which drew the largest audiences were medicine, surgery and obstetrics. The number in attendance at each exercise has been kept by the Committee of Arrangements for future reference.

There was a large attendance at the Council Meeting and the routine business of acting on the designated subjects was carried through as promptly as possible. Valuable information with suggestions for endorsement of resolutions or recommendations which were not of a controversial nature were submitted by several of the committees. Those presented by the Committee on State and National Legislation were so extensive, dealing as

they did with matters before the state legislature and Congress, that there was room for differences of opinion as to procedure. So far as state matters are concerned, the chairman reported success in overcoming unapproved bills but inability to secure legislative approval of all those measures which had been endorsed by the Council. He then made a detailed report of the situation with respect to the Wagner Bill and the conferences which had been held with the Massachusetts senators and with representatives of the American Medical Association. There were various suggestions as to the proper procedures to be followed in efforts to remove from the Wagner Bill those features which are inimical to the interests of the profession, and as a reflection of these differences of opinion, the nominations of the President for members of the Committee on State and National Legislation for the ensuing year were not unanimously acceptable and others from the floor were presented; this was followed by a vote by ballot for members of the committee. The result was not announced until the afternoon; the members of the new committee are Drs. Charles C. Lund (chairman), Earle M. Chapman, Brainard F. Conley, David L. Lionberger and Charles A. Robinson. All other committees were duly elected without contest.

On nominations by the committee acting under the provisions of the by-laws the following designated officers were elected to serve for the ensuing year: president, Dr. Walter G. Phippen, of Salem; vice-president, Dr. A. Warren Stearns, of Billerica; secretary, Dr. Alexander S. Begg, of Boston; treasurer, Dr. Charles S. Butler, of Boston; and orator, Dr. W. Jason Mixter, of Boston.

The proposed changes in the by-laws, copies of which had been sent to the councilors, were presented for action. With the exception of Amendment 4 and its corollary, Amendment 6, which were not approved, and a change in the wording of Amendment 3, the list was approved and forwarded to the annual meeting of the Society for final disposition.

Three hundred and thirty-two fellows and guests participated in the annual dinner at the Hotel Bancroft, Wednesday evening. The postprandial exercises included the distribution of the prizes awarded to the golfers by the president, with appropriate witty comments, and an address by Mayor Bennett, of Worcester. The latter assured the Society of his appreciation of the honor conferred in the selection of the "Heart of the Commonwealth" for an annual meeting and, after urging doctors to devote more time to civic responsibilities thereby bringing to bear the influence of educated citizens on municipal problems, he cordially invited the Society to make Worcester its meeting place as often as possible. The orator of the occasion was the Honorable Henry Parkman, Jr., corporation counsel for the City of Boston and general chairman of the Tufts College Medical School Development Program. In regard to the latter, which is committed to the education of general practitioners for rural communities and also to such postgraduate instruction as may be needed by doctors of advanced age living away from medical centers, he explained the close association of Tufts College Medical School with the New England Medical Center, of which the Boston Dispensary is an integral part. All the details of this department were set forth and prominence was given to the provisions for substitutes who are assigned to fill the positions held by practitioners who wish to spend a month at the medical center for studying modern diagnostic methods and the latest advances in treatment. Credit was given to Tufts College Medical School for taking a forward step in meeting an obvious social obligation.

At the conclusion of the scientific program the annual meeting was called to order by the president, Dr. Channing Frothingham. The incoming president, Dr. Phippen, was introduced and, in response, assured the Society of his appreciation of the honor conferred on him and asked for the co-operation of every member in carrying forward the functions of the Society. The secretary, Dr. Begg, reported that the membership of the Society is now 5432, a gain of 127 over that of last year. He read the several amendments to the by-laws which had been approved by the Council; the approval of the Society was voted. The Presi-

dent then read his report on the state of the Society, in which he reported that the financial condition is sound and well managed by the treasurer, Dr. Butler, and that the committees of the Society had diligently and faithfully carried on the tasks assigned to them. Explanations were given of changes which had taken place in the personnel of these committees. Comments on the important problems before the profession were submitted.

The orator, Dr. Elliott P. Joslin, then read the annual discourse, in which he dealt with the many phases of "social medicine," words which he preferred to use rather than those of "socialized medicine." This included many of the social, economic and professional functions connected with plans for dealing with the health of the people. The latter part of his address was devoted to a consideration of medical education and the quality of the physicians who are to take the places brought about by the yearly loss of active practitioners. This address will interest all members of the Society who are conversant with problems connected with medical education and professional responsibilities relating to the health of the people and should stimulate discussions of the implications of the propositions outlined by the author.

It is hoped that these brief comments on the annual meeting will induce the fellows of the Society to read the official reports of the proceedings which will be published in the *Journal* at an early date.

A POSTGRADUATE TOUR IN THE SEVENTEENTH CENTURY

When Edward Browne, the son of Sir Thomas Browne, returned from Cambridge University to his father's house in Norwich at the age of nineteen, with his M.B. degree, he, like many other medical students, was disturbed about his future. Should he go to London for hospital work, wait for practice at home, or spend his time in his father's ample and hospitable library, reading botany, literature, medicine and theology? He chose the latter course and supplemented his reading with daily dissections of animals. He saw at least one patient and received his first fee of ten shillings. Later he attended a few lectures at St. Bartholomew's Hospital in London and vacationed in Italy and France. He was elected a fellow of the Royal Society when he came of age, largely, one presumes, on his father's reputation.

At the age of twenty-three he took up traveling in earnest and for the next five or six years spent most of his time in Europe. His observations were published in two short books, *A Brief Account of Some Travels* (London, 1673) and *An Account of Several Travels* (London, 1677). Both were reissued in a sumptuous second edition, this time one volume in folio (London, 1685). This edition is, in all respects, the best book of the three.

Browne was an accurate and painstaking observer, but his style of writing was dull, and the first book is hardly more than a catalogue of towns, buildings and matters of historical interest. The second book was a little more lively, and there are interesting descriptions, such as that of the Imperial Library at Vienna, its contents and his friendship with the librarian, Lambecius. Browne made a few gifts to the library and gained, through the librarian, a formal pass from Emperor Leopold, exempting him from customs on the way back to England. In Thessaly he remained for some time at Larissa, visualizing the Hippocratic country, but one can hardly agree with Norman Moore* that Browne "followed in imagination the practice of Hippocrates." In none of his writings, moreover, is the depth found that was so characteristic of his father's works.

On his return from his travels, Browne practiced in London and became surprisingly successful. In addition he wrote the earliest known copy of the *Pharmacopoeia of St. Bartholomew's Hospital* (London, 1670).

*Moore, Norman. Edward Browne (1644-1708). *The Dictionary of National Biography*. Vol. 3. New York: The Macmillan Co., 1908. P. 42.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

LATE POSTPARTUM HEMORRHAGE

Mrs. N. L., thirty-five-years old, was readmitted to the hospital on December 15, 1938, twenty-six days after the normal delivery of her first baby, with a chief complaint of vaginal bleeding.

The family history was essentially negative. The patient had had a cholecystectomy and appendectomy seven years previously. In December, 1937, she had had a complete miscarriage at approximately the sixth week of pregnancy. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted three days without discomfort. Her last menstrual period was January 30, making her due for delivery November 6.

She was seen regularly in the prenatal clinic of the hospital from the fifth month of her pregnancy, and at no time were there abnormal signs or symptoms.

On the afternoon of November 19, the patient was admitted to the hospital in active labor. During the first stage of labor 6 gr. of Nembutal were given. At 10:30 p. m. a normal living infant in ROA position and weighing 7 pounds, 12 ounces, was delivered spontaneously. An ampule of Pitocin was given subcutaneously. While awaiting the expulsion of the placenta and membranes, which, when delivered, appeared to be intact, a first-degree laceration of the perineum was repaired. Blood loss was estimated at 350 cc. Following expulsion of the placenta, 1/320 gr. of Ergotrate was administered subcutaneously, after which the uterus contracted firmly. The fundus was held for an hour. Tablets of Ergotrate (1/320 gr.) were given every four hours for six doses. The puerperium was uneventful. The discharge note, made on December 1, read: "General condition good; uterus well involuted, anterior, freely movable, non-tender; perineum healed, relaxed; cracked nipples; lochia alba, slight; vaults non-tender and free of masses."

On December 15, two weeks after discharge, the patient was readmitted to the hospital as stated above. She described an initial profuse hemorrhage occurring December 8, followed by intermittent spotting until the evening before admission when another profuse hemorrhage occurred. Her family physician referred her back to the hospital. The temperature was 98.6°F., the pulse 76, the respirations 20, and the blood pressure 106 systolic, 70 diastolic. On physical examination there were a well-healed scar in the right upper quadrant, tenderness without spasm in both lower quadrants, a midline smooth rounded mass palpable just above the symphysis pubis, and vaginal bleeding of a slight degree. The red-blood-cell count was 3,870,000 with 75 per cent hemoglobin, and the white-blood-cell count 13,300. Urinalysis revealed a specific gravity of 1.028, an acid reaction, a trace of albumin, no sugar, gross blood, and many red cells and an occasional white cell in the sediment.

The patient was placed in Trendelenburg position and the vulva prepared. An ice bag was placed on the lower abdomen. A quarter grain of morphine and an ampule of Ergoklonin were administered subcutaneously. Morphine (1/6 gr.) was given every four hours for four doses; Ergotrate (1/320 gr.) was given every four hours for five doses. A four-hour chart with blood pressure readings was kept. Bleeding ceased altogether on December 19 and did not recur. The temperature remained normal, and the pulse never rose over 90 during the hospital stay. On December 24, the patient left the hospital. The uterus was well involuted, and no recurrence of bleeding occurred.

Comment. It is perfectly possible that the severe bleeding that occurred on December 8 and December 14 may have been caused by the retention and separation of a small piece of placenta and that the bleeding on December 15 at the time of admission was accompanied by the complete expulsion of all pieces of retained tissue. It is uncommon for bleeding such as this to occur unless associated with some form of retained products; however, it is very common for the first period after any delivery to be extremely excessive and occasionally so excessive that curettage becomes a necessity. Subinvolution is more frequently associated with continued dribbling than with excessive hemorrhage. Conservatism in the handling of this case after re-entry was stimulated by the fact that the bleeding had practically ceased, and it is quite probable that if the bleeding had recurred the uterus would have been invaded.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

MISCELLANY

TUBERCULOSIS IN INDUSTRY

To what extent tuberculosis may be regarded as an industrial hazard is engaging the attention of industrial leaders, legislators and physicians. Not only occupation but also several other factors are responsible for tuberculosis among industrial workers. Ornstein and Ulmar

(Tuberculosis in industry. *Quart. Rev. Sea View Hosp.* 4:164-181, 1939) analyze these factors. Excerpts from their paper follow.

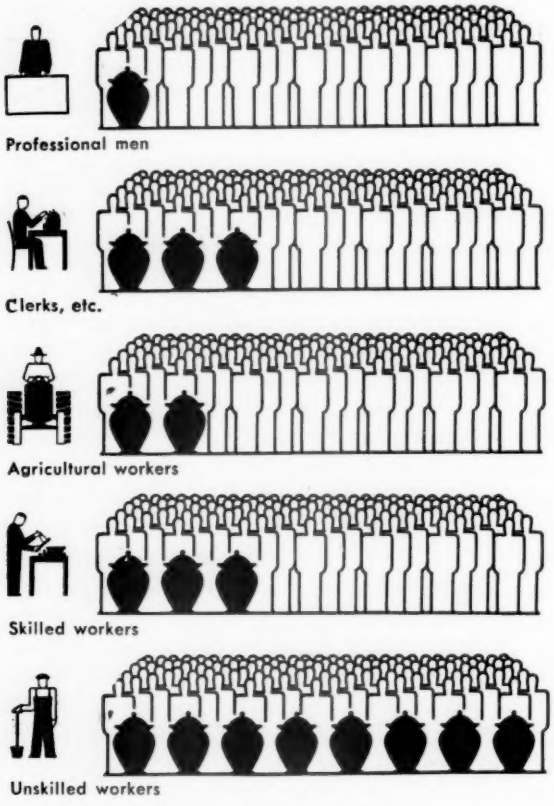
The death rate among the unskilled workers is more than twice that of the skilled workers. Is this due to the industry or to lesser earning capacity? It is more probably due to the latter.

Is tuberculosis an occupational disease? An occupational disease is one that arises out of the occupation per se. There must be a definite relation between the etiology of the disease and the occupation. The frequency of the occurrence of the disease in the occupation must be greater than the incidence of the disease in a similar group not so employed. A high frequency of tuberculosis in a particular industrial group may be due to the fact that the labor is recruited from a section of the city where tuberculosis is more prevalent than it is in other sections. Unskilled labor comes chiefly from those parts of the city where the tuberculosis death rate is high.

In a few definite groups only may tuberculosis be considered as an occupational disease. These groups include:

Workers caring for the tuberculous sick — nurses, orderlies, attendants, and so forth. The frequency of the occurrence of tuberculosis infection and disease among medical students and nurses has been noted by numerous workers. There can be no question but that the opportunity for exogenous infection of the lungs by the tubercle bacillus presents itself in the care of the tuberculous sick. At Sea View Hospital, New York City, x-ray evidence of pulmonary tuberculosis was found in 10 of the 1000 nurses during the period from 1930 to 1935, and 21 others developed lesions in the lungs while working in the hospital. Of the 10 cases which showed evidence of disease on admission, 7 continued to work with either clearing or no change in the lesion; 1 broke down with a cavity and 2 did not start work. It is most important to note that while the incidence rate was low in the Sea View group (1 per cent) the occurrence rate was high, which indicates a definite hazard from an insurance standpoint. By contrast, the tuberculosis occurrence rate among employees of a large department store was found to be a small fraction as compared with that of the nurses group.

Occupation Influences Tuberculosis



Each urn: 25 deaths from tuberculosis per 100,000 workers in the age of 25 to 44 years.

N. T. A. Isotype Chart

Similar studies made among medical students have tended to show an increased incidence of tuberculous disease among them, presumably due to their occupation, which throws them in contact with open tuberculosis cases.

In a great many general hospitals, the frequency of implantation of tubercle bacilli in the previously non-infected probationers has been almost as great as that in the tuberculosis wards. Many cases of open tuberculosis are admitted to the general hospital for surgical and other forms of treatment. The tuberculous disease is not suspected and the nurse takes no precautions against exogenous cross-infection while she attends the patient. The contact may be a continuous one without the tuberculous disease ever being discovered. The nurse later breaks down with the disease. The question of whether the tuberculosis acquired in a general hospital is an occupational disease will depend a great deal on the frequency of the admission of the tuberculous to the hospital.

Store clerks, saleswomen, waiters, conductors and others who have contact with a large number of people in whom there may be a high incidence of tuberculous disease. The presumption that the tuberculosis acquired in these occupations may be classed as occupational is based on the many opportunities for contact with open cases of pulmonary tuberculosis. There must be a wide variation in the opportunities of contact infection in districts with small or high incidence of clinical tuberculosis. Think of the possibility of such contact in the 5 and 10 cent stores in neighborhoods of low economic standards. There are no definite figures as yet in such industries but the general impression is that the occurrence is frequent. The workers are not recruited from the slum sections; in some of the large cities they come from a good middle class where the incidence is not high.

Workers exposed to silica dusts. Silicosis is definitely an occupational disease. Many investigators have associated silicosis with the occurrence of pulmonary tuberculosis, but the authors dispute the commonly accepted belief that the deposit of silica in the lungs renders the lungs susceptible to infection by tubercle bacilli. That most of the silicotics die of pulmonary tuberculosis is a debatable question.

The present concept of the high mortality of tuberculosis is founded, not on extensive autopsy series, but rather on the computations of vital statistics. This is a source of grave error, for not only can mistakes in diagnosis be made by the clinician so that the basis of the statistics is wrong, but also misleading conclusions can be drawn from the existing figures.

The authors warn of the dangers of error in differentiating between silicosis and pulmonary tuberculosis, challenge the high frequency and death rate of tuberculosis as a complication of silicosis and assert that clinical tuberculosis should not be diagnosed in silicosis unless tubercle bacilli are demonstrable in repeated sputum examinations.

Workers exposed to trauma. Compensation laws have

directed attention to the relation of trauma to tuberculosis. Tuberculosis has a specific etiology and, therefore, trauma cannot produce the disease. Trauma can, however, reactivate a previously existing active tuberculosis. Most of the confusion comes from the varied opinion concerning the time interval which may elapse from the date of the injury to recognition of the tuberculous disease.

Gases and vapors may also activate a pre-existent pulmonary tuberculosis by producing an inflammatory process in the vicinity of the pre-existing disease by irritant chemicals.

Trauma plays an important role in tuberculosis of organs other than the lungs. In this group the time element creates difficulties because of the inability to demonstrate the immediate spread of tuberculosis. Reprinted from *Tuberculosis Abstracts,* June, 1939.

NOTE

Dr. Douglas A. Thom, professor of psychiatry at Tufts College Medical School, was elected president of the American Psychopathological Association at its recent meeting in Atlantic City. He succeeds Dr. Abraham Myerson, who was elected to the council.

CORRESPONDENCE

AN AMERICAN HEALTH-INSURANCE PLAN

To the Editor: This plan compels the man or woman on salary to save in the savings department of a bank. A certain amount, estimated at 4 per cent of the salary, is earmarked and only used for sickness and accidents to pay the hospitals, physicians, nurses, dentists and druggists. This takes in every man and woman on salary and should be handled directly by the employer who places the money on deposit in the bank in the name of the employee.

It does not put the medical or dental profession into politics or allow control of the professions by the Government. It does not increase the number of government employees, nor does it put an increased burden on the Government or professions. It will decrease taxation as there will be fewer charity patients in the federal, state, county and city hospitals, since their compulsory savings make them financially independent; also it will help other hospitals for the same reason.

This fund cannot be used for automobiles, gay parties or gambling. The compulsory part of this deposit should accumulate as long as the employee is working. The employee should receive interest as in a savings account, to be added to the principal or withdrawn as he sees fit. Any person not on salary should be allowed to deposit in the same way. On the death of the employee this deposit would act as a life insurance after all bills are paid.

This will tend to prevent the isms in government — Communism, Fascism, and so forth — and show the people the way to save.

ARTHUR N. MAKECHNIE, M.D.

14 Upland Road,
Cambridge, Massachusetts.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in in our letter of May 2 the following have been accepted:

Calco Chemical Co., Inc.
- Sulfapyridine — Calco
  - Tablets Sulfapyridine — Calco, 0.5 gm. (7.7 gr.)

Lederle Laboratories, Inc.
- Sulfapyridine — Lederle
  - Tablets Sulfapyridine — Lederle, 0.5 gm. (7.7 gr.)

Eli Lilly & Co.
- Estriol — Lilly
  - Pulvules Estriol, 0.06 mg.
  - Pulvules Estriol, 0.12 mg.
  - Pulvules Estriol, 0.24 mg.
- Estrone — Lilly
  - Ampules Estrone in Oil, 0.1 mg.
  - Ampules Estrone in Oil, 0.2 mg.
  - Ampules Estrone in Oil, 0.5 mg.
  - Ampules Estrone in Oil, 1.0 mg.
  - Suppositories Estrone, 0.2 mg.

Merck & Co., Inc.
- Riboflavin — Merck
  - Ampules Riboflavin — Merck, 10 mg.
  - Ampules Riboflavin — Merck, 100 mg.
  - Riboflavin — Merck, 1 gm. bottle.
- Sulfapyridine — Merck
  - Tablets Sulfapyridine — Merck, 0.5 gm. (7.7 gr.)

PAUL NICHOLAS LEECH, *Secretary.*

535 North Dearborn Street,
Chicago, Illinois.

REPORT OF MEETING

HARVARD MEDICAL SOCIETY

At the regular meeting of the Harvard Medical Society on Tuesday, February 28, in the Peter Bent Brigham Hospital amphitheater, Dr. W. T. Salter presided. The program was opened by the presentation of two cases.

The first case, from the surgical wards and presented by Dr. Fred Lesemann, was that of a thirteen-year-old boy who was brought in following a coasting accident in which he ran into a tree and injured his left side. There was no loss of consciousness, only pain. Physical examination revealed an acutely ill boy breathing rapidly and distressfully. There was a small contusion over the ribs in the left posterior axillary line. Hyper-resonance with decreased breath sounds and absent tactile fremitus was found over the left chest, and the heart and mediastinum were displaced to the right. X-ray examination confirmed the diagnosis of hydropneumothorax. A trocar allowed evacuation of blood and air, with considerable relief to the patient. For the next thirty-six hours there was drainage of a moderate amount of blood. The temperature began to rise and remained in the vicinity of 104°F. rectally for eleven days. *Staphylococcus aureus* was cultured from the drainage tube. One hundred to two hundred cubic centimeters of purulent material was drained, following which the temperature began to subside, and since then, drainage under water has been followed by an increase in the lung shadow and a decrease in the fluid shadow by x-ray.

Dr. Robert Gross mentioned the two ways in which traumatic rupture of the lung can occur: either as a result of fractured rib tears, or spontaneously when the glottis, diaphragm and rib cage are held rigidly fixed. The flap of torn lung tissue acts as a valve, trapping inspired air which collects in a few hours and forces the mediastinal contents over. It is a real emergency. The chest can be aspirated, or it may be necessary to open it surgically and allow the injured lung to remain collapsed until it heals. Dr. O'Hare brought out the point that cases have been cited as having been caused by yawning or stretching.

The medical case was presented by Dr. Albert C. England. A thirty-five-year-old man was admitted for a check-up on his high blood pressure. In November, 1938, he had had an attack of intestinal grippe, and the local physician had told the patient his blood pressure was very high, advised him to go on a low-protein diet and gave him some medication; the patient kept on with his work. One week previously, which was two days before entry, the patient had a similar attack of abdominal cramping pains and decided to go to the hospital. Physical examination of the ocular fundi showed marked papilledema; the arteries were thickened and tortuous, and arteriovenous nicking was demonstrable. There were white exudates in a radiating star pattern at the maculas. His heart was moderately enlarged, extending 14 cm. out in the sixth left interspace, and there was a Grade 2 systolic murmur. The second aortic sound was loud and ringing. His blood pressure was 235 systolic, 160 diastolic, and slightly higher in the leg. The lungs were clear, the liver normal, and there was no edema. Urinalysis revealed a specific gravity of 1.010, none to a very slight trace of albumin, casts and cells. The red-blood-cell count was 5,000,000 with 70 per cent hemoglobin; the stools were guaiac negative; the phenolsulfonephthalein test gave a value of 45 per cent in two hours and ten minutes; the serum nonprotein nitrogen was 31 mg., the total protein 6.5 gm., the albumin 3.8 gm., and the globulin 2.7 gm. per 100 cc. The patient has been quite comfortable. The diagnosis was malignant hypertension.

The main part of the program of the evening was given over to Drs. Roger W. Robinson and James P. O'Hare. Dr. Robinson presented the paper: "Further Experiences with Cyanate Therapy in Hypertension."

Briefly reviewing the work done on this subject, Dr. Robinson stated that in 1901 sodium cyanate was first tried because of its similarity in action to that of the bromides, which are used in sedation and show a side effect in reducing hypertension. In 1925 Nichols revived interest in the drug but found nothing to recommend it because of its serious toxic effects. The dosage used at the time was 0.6 gm. daily. In 1931, Dr. O'Hare and others tried the drug and found it lowered blood pressure in only 2 of 25 cases and produced toxic symptoms in almost all of them. Finally, Barker in 1936 discovered that, by maintaining an effective blood concentration of 6 to 10 mg. per 100 cc., lowering of pressure could be obtained and toxicity avoided. He discovered that there was a very large factor of individualization of dosage, and explained on this basis the previous failures cited above. Forty-five patients were treated by him with enthusiastic results. Dr. O'Hare decided to give it another try. The method of experimentation consisted in establishing a three-month control period, followed by three months of medication, and succeeded by another control period in which the drug was removed from the vehicle without the patient's knowledge — to avoid psychotherapeutic effects. Of 15 patients, 10 showed a significant drop in blood pressure and cessation of headaches. These results were reported in the *New England Journal of Medicine* (*219:736–740, 1938*). Since then the work has been extended until at this reading the results on 75 patients are available.

Because of the known toxic action of cyanate, complicated cases of vascular hypertension were, by and large, avoided. However, 4 of the 75 had had strokes, 1 had had angina pectoris, 1 a mild decompensation and 1 nephritis with impaired renal function. These 7 were treated very conservatively. All the patients were placed on the usual hypertensive regimen and had a control period of three months, during which sedation alone was given. Thirty-three patients were followed for one year. Preliminary dosage consisted of 0.2 gm. three or four times a day for three or four days. Following this the cyanate in the blood was determined, and the optimum dose was usually found to be 0.2 gm. twice a day, estimated on the basis of the cyanate level and the blood pressure. Often, a satisfactory level, namely, one in which there was a good drop in blood pressure without toxic signs, could be maintained by doses as low as 0.2 gm. twice a week. The known cyclical nature of blood-pressure readings in hypertension was taken into account, and psychological factors were evaluated, so far as possible.

Eighty-eight per cent of the cases showed a drop in systolic pressure of at least 30 mm. of mercury, and 11 per cent 60 mm. or more; 62 per cent had a diastolic drop of 20 mm., 16 per cent of 30 mm. Three cases had a drop of 100 mm. systolic, 35 mm. diastolic, for five months. One case, that of a young woman, has been on a cyanate regime for a year with good results. There were 9 cases with no drop in blood pressure: 3 of these in young patients with high diastolic pressures, 2 in elderly patients with arteriosclerosis, 3 in which the treatment was discontinued because of reactions, and 1 which was not adequately treated. The lowest blood-pressure readings corresponded with the highest blood-cyanate levels and conversely. The usual marked fluctuations of blood pressure in such cases were much reduced by cyanate. Eighteen out of 20 had complete relief from hypertensive headaches.

There are many reasons that might explain these results: such as an effect on the heart muscle, vasodilatation, lowering of blood viscosity by reducing its fibrinogen or total protein content, or a decrease in the oxygen consumption of all body tissues.

Twenty-nine patients exhibited toxic symptoms of one type or another. Of these, 23 cases were classified as mild. Weakness and lack of energy were the most frequent symptoms, occurring in 12 cases. In only 2 were they severe enough to require abatement or cessation of therapy. An experiment in the oxygen consumption of liver tissue offered a probable explanation for this weakness. It was noted that as the concentration of cyanate in the blood increased, the oxygen consumption decreased.

Skin manifestations of toxicity manifested themselves either as macular erythematous patches or as a rash simulating seborrheic dermatitis. Some patients gave reactions due to special sensitivity to the drug. Some had the rash only when drug resistant and, therefore, a blood-cyanate concentration of 12 to 17 mg. per 100 cc. was maintained. Such rashes were transient, disappearing when the dose was decreased. One patient, however, had a generalized exfoliative dermatitis, a serious complication, but recovered. Three cases had areas of purpura during treatment, and an increased tendency to bleed.

Two male patients reported a decrease in libido.

There has been a question of the production of thrombosis following the lowered blood pressure, but to date no myocardial damage as a result of cyanate therapy has been proved. One elderly patient, however, had an attack of angina pectoris when his blood pressure dropped from 290 to 210 mm. Another patient, aged sixty-two years, with angina and an extremely high blood pressure, was successfully treated with cyanate. However, eleven months later he had a sudden hemiplegia. Whether the cyanate produced this by lowering the pressure too much was not certain, but seemed unlikely in view of the fact that its general level was 198 systolic, 108 diastolic.

One case of congestive heart failure occurred in a pa-

tient who was on digitalis therapy for previous myocardial failure. In the seventh week of cyanate treatment, the blood pressure having been reduced from 240 systolic, 140 diastolic, to 150 systolic, 100 diastolic, nocturnal dyspnea and rales appeared. Treatment was stopped, and the signs disappeared. One year later the patient died of a cerebral accident, with a blood pressure of 250 systolic, 130 diastolic.

Three patients developed hallucinatory psychoses: the first at a blood-cyanate level of 10 mg. per 100 cc., having had a control systolic pressure of 275 mm.; the second at 14 mg., after having had no drop after one month of therapy from the control systolic pressure of 300 mm. (a true cyanate intoxication); the third overdosed herself to a blood-cyanate level of 24.9 mg., her pressure having dropped from 250 systolic, 140 diastolic, to 200 systolic, 100 diastolic. The last patient returned to normal mentality in three weeks, when the cyanate level had been reduced to 15 mg.

Five of these 6 patients with serious effects were over fifty-five years of age. All had a very high degree of hypertension, and 4 of them had had previous serious episodes such as "strokes," angina pectoris, heart failure, and so forth. It is to be concluded, therefore, that the choice of patients for cyanate therapy must depend on their having uncomplicated essential hypertension, preferably under the age of sixty. A blood-cyanate level of 14 mg. per 100 cc. should be the absolute maximum, whereas a lower concentration should be maintained if possible. Finally, if there is a poor effect following a level of 10 to 14 mg. for from two to four weeks, administration of the drug should be stopped. Carefully controlled, cyanate therapy is of definite value, in Dr. Robinson's opinion.

In opening the discussion of Dr. Robinson's paper, Dr. O'Hare's comment was that, although cyanate therapy in carefully selected cases of hypertension offered more than did any other therapeutic method, it is not the ideal remedy because of the drug's toxicity. Until a better method is available it will serve a very useful purpose.

Dr. Samuel Levine asked about the effect of cyanate on Goldblatt dogs, to which Dr. Robinson quoted Barker's results showing no effect. It was said that, at the Massachusetts General Hospital, good results with cyanate therapy had been obtained in 2 cases out of a small series of 29.

Dr. Robinson, in answering questions put to him, replied that the symptom of weakness was often temporary, disappearing when the patient became adjusted to the lower blood-pressure level. He added that cyanate resistance, so-called, is a doubtful entity, since patients are responsive the second time the drug is tried after resistance to the first attempt.

NOTICES

REMOVAL

FRANCIS J. MCNAMARA, M.D., announces the removal of his office to 106 West Foster Street, Melrose.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Wednesday, June 21, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 o'clock noon.

The program, under the auspices of the laboratory department, will begin at 12:30 p. m.

Laboratory Diagnosis of Rabies. Dr. William A. Hinton.

Some Vascular Measurements in Hypertension. Dr. Harold E. MacMahon.

A Fatality From Acute Hemolytic Anemia Which Developed During the Administration of Sulfanilamide. Dr. Harold Wood.

All interested in the subject are cordially invited to attend.

ROBERT W. BUCK, M.D., *President,*
JAMES M. BATY, M.D., *Secretary.*

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, June 27, at 12 o'clock noon. Dr. Auerbach, pathologist, Sea View Hospital, New York City, will speak on "Pathogenesis and Management of Tuberculous Pleural Empyema" and will show lantern slides.

Physicians are cordially invited to attend.

JOHN B. HALL, M.D., *Secretary.*

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in Andrew Carney Assembly Room on Monday, June 19, at 11:30 a. m.

PROGRAM

Case reports.

Highlights of Recent Conventions:

American Gynecological Society and American Medical Association. Dr. L. E. Phaneuf.

American Association of Genito-Urinary Surgeons. Dr. R. C. Graves.

American Urological Association. Dr. C. J. E. Kickham.

Physicians and medical students are cordially invited to attend.

ROY J. HEFFERNAN, M.D., *Secretary.*

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The American Board of Obstetrics and Gynecology announces that at the recent examinations held by the Board at St. Louis, Missouri, on May 13, 14, 15 and 16 two hundred and fifty-nine candidates were examined. Two hundred and twenty-eight candidates were successful in the examinations and were certified by the Board, twenty-nine candidates failed, and two examinations were not completed by the candidates.

At the annual meeting of the Board, held in St. Louis on May 12, it was found necessary, on account of increased administration expenses, to increase the application and examination fees. Effective immediately, these are to be as follows: application fee $15.00, payable on submission of application for review by Board; examination fee $75.00, payable on notification to candidate of acceptance of the application and assignment for examination. Neither fee is returnable. This increase does not apply to candidates whose applications were filed prior to May 12, 1939.

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, December 2, 1939, at 2:00 p. m. *The Board announces that it will hold only one Group B, Part I, examination in this and subsequent years.* Candidates who

successfully complete the Part I examination proceed automatically to the Part II examination held later in the year.

Applications for admission to the Group B, Part I, examination must be on file in the secretary's office not later than October 4, 1939.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting in Atlantic City, New Jersey, on June 7, 8 and 9, 1940, immediately prior to the annual meeting of the American Medical Association to be held in New York City from June 10 to 14, inclusive.

Applications for admission to the Group A, Part II, examination must be on file in the secretary's office not later than March 15, 1940. For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

"CARLO FORLANINI" SCHOLARSHIPS

The International Union against Tuberculosis announces that six scholarships for advanced study in tuberculosis at the "Carlo Forlanini" Institute in Rome have been made available to the Union through the Italian Fascist National Federation.

These competitive scholarships, of a value of 2000 liras, respectively, plus board and lodging, are intended to enable foreign medical practitioners to stay at the "Carlo Forlanini" Institute in Rome for the purpose of following a course of studies. This stage of eight months will correspond with the academic year (from November 15 to July 15) including the usual holiday periods. The scholars will reside at the Institute.

The scholarships will preferably be awarded to young physicians who are already familiar with tuberculosis problems and who wish to improve their knowledge of this branch of medicine.

The kind of work undertaken at the Institute will be subject to an agreement between the director of the Institute and the candidate.

Papers resulting from this work must be submitted for publication in the first instance to the editor of the *Bulletin of the International Union against Tuberculosis.*

The scholarships will be awarded at the next session of the Executive Committee which will meet in Berlin in September, 1939. The names of candidates, accompanied by particulars as to their age, qualifications and professional experience, must be forwarded to the Secretariate of the Union, 66, boulevard Saint-Michel, Paris (6e), not later than July 15.

No candidature shall be taken into consideration unless it has been forwarded to the Executive Committee by a government or an association belonging to the International Union.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, June 19

Monday, June 19

•11:30 a. m. Carney Hospital monthly clinical meeting and luncheon.

Tuesday, June 20

•10 a. m. - 12:30 p. m. Boston Dispensary tumor clinic.

Wednesday, June 21

•12 m. Boston Dispensary luncheon meeting of the clinical staff.

Friday, June 23

•10 a. m. - 12:30 p. m. Boston Dispensary tumor clinic.

Saturday, June 24

•10 a. m. - 12 m. Staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

•Open to the medical profession.

June 19 — Carney Hospital monthly clinical meeting and luncheon. Page 1019.

June 20 — Lawrence Cancer Clinic. Page 977, issue of June 8.

June 21 — Boston Dispensary luncheon meeting of the clinical staff. Page 1019.

June 26-29 — National Tuberculosis Association. Page 897, issue of May 25.

June 27 — South End Medical Club. Page 1019.

June 27-29 — Medical Library Association. Page 941, issue of June 1.

June 29 — Pentucket Association of Physicians, 8:30 p. m., Hotel Whittier, 5 Washington Street, Haverhill.

August 30 - September 2 — Seminar in Physical Therapy. Page 857, issue of May 18.

September — Boston Psychoanalytic Institute. Page 450, issue of September 22.

September 4-6 — Institute for the Consideration of the Blood and Blood-Forming Organs. Page 941, issue of June 1.

September 5-8 — American Congress of Physical Therapy. Page 857, issue of May 18.

September 11-15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

September 14-16 — Biological Photographic Association. Page 941, issue of June 1.

September 15-28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

October 23 - November 3 — New York Academy of Medicine. Page 977, issue of June 8.

Fall, 1939 — Temperature Symposium. Page 218, issue of February 2.

December 2 — American Board of Obstetrics and Gynecology. Page 1019.

May 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

June 7, 8, 9, 1940 — American Board of Obstetrics and Gynecology. Page 1019.

BOOKS RECEIVED FOR REVIEW

Chronic Arthritis. Robert T. Monroe. Edited by Henry A. Christian. 84 pp. New York, London and Toronto: Oxford University Press, 1939. $2.00.

Diseases of the Nose and Throat. Charles J. Imperatori and Herman J. Burman. Second edition revised. 726 pp. Philadelphia, London and Montreal: J. B. Lippincott Co., 1939. $7.00.

The Mental Hygiene Movement: From the philanthropic standpoint. 73 pp. New York: Central Hanover Bank and Trust Co., 1939.

Textbook of Medicine. By various authors. Edited by J. J. Conybeare. Fourth edition. 1112 pp. Baltimore: The Williams & Wilkins Co., 1939. $6.75.

Medical Microbiology. Kenneth L. Burdon. 763 pp. New York: The Macmillan Co., 1939. $4.50.

Cancer Handbook of the Tumor Clinic, Stanford University School of Medicine. Edited by Eric Liljencrantz. 114 pp. Stanford University: Stanford University Press, 1939. $3.00.

Rural Medicine: Proceedings of the conference held at Cooperstown, New York, October 7 and 8, 1938. 268 pp. Springfield, Illinois and Baltimore: Charles C Thomas, 1939. $3.50.

Fluorine Intoxication: A clinical-hygienic study with a review of the literature and some experimental investigations. Kaj Roholm. 364 pp. London: H. K. Lewis & Co., 1937. 20s.

BOOK REVIEWS

Alcohol in Moderation and Excess: A study of the effects of the use of alcohol on the human system. J. A. Waddell and H. B. Haag. 184 pp. Richmond: The William Byrd Press, Inc., 1938. $1.00.

This is an interesting book and one that physicians might well inspect. It reports a study made at the direction of the General Assembly of Virginia in 1936. It was rejected by the Assembly and was published later by two of the original compilers. The purpose of the study was that scientific findings concerning alcohol be made available to citizens of Virginia and that these findings be used as a basis for material taught in public schools of Vir-

ginia. The book aims at furnishing the lay reader with unbiased findings and compilations from the best medical and scientific sources of the past two decades.

This book is just not another book on alcohol, but rather it offers an appeal to reason, judgment and intelligence from the medical, psychological and general hygienic aspects. Alcohol is not presented as a moral issue, though the effects of overindulgence on morals and behavior are not slighted. The book reports simple, concise facts regarding the effects of the use and abuse of a most important drug. It is an unprejudiced textbook relative to the physiological and psychological effects of alcohol. A few popular theories are exploded. The study presupposes an elementary knowledge of anatomy and physiology. Individual differences in susceptibility are stressed, as well as individual tolerance.

Statistical data are not given in detail but are summarized and analyzed in some cases to representative figures from national and local governmental authorities. The chapter on statistics is divided as follows: the supply and consumption of alcohol; drunkenness; accidents in their relation to alcohol; automobile accidents and non-automobile accidents; crime in relation to alcohol; alcoholic mental diseases; mortality from alcohol.

This book emphasizes the facts that education is necessary in solving the problem of alcohol and that sobriety cannot be legislated nor can fear be used to influence public attitudes as regards the use of alcohol. It is indicated that the process of education must be informative and without bias and prejudice.

The last chapter is devoted to opinions of eminent specialists covering the crucial topics concerning alcohol and the human body.

The glossary is well arranged and explains many of the technical terms used in the text.

Adventures in Respiration: Modes of asphyxiation and methods of resuscitation. Yandell Henderson. 316 pp. Baltimore: Williams & Wilkins Co., 1938. $3.00.

This volume is essentially a scientific autobiography. In it the author reviews his lifelong study of the physiology and pathology of breathing, and the practical application of the principles derived therefrom. The story covers a period of thirty years or more. It is written in that inimitably emphatic, yet good-natured, style which is characteristic of Professor Henderson. Often criticized, he yet remains always cordial to his critics, which is more than can be said of some scientists.

His major thesis, and one first advanced by him at the beginning of his professional career, is that acapnia, or deficiency of carbon dioxide, which leads in turn to anoxia, or a deficiency of oxygen, is a factor of importance in many ills and adversities encountered by the human organism, as, for example, the depression of vitality after anesthesia, surgical operation, traumatic shock or severe illness of various sorts. He intimates that, whereas he was never able to sell this theory to the intellectuals, nevertheless the present-day general use of carbon dioxide in the operating room and hospital ward gives it considerable vindication.

A prerequisite for living is an adequate supply of oxygen. "An exclusion of oxygen extinguishes a fire, so too in a man or animal a deficiency of oxygen in the blood and tissues induces death in asphyxia." In dealing with the problems of asphyxia, however, the author emphasizes that acapnia must be considered as well as anoxia for the reason "that a diminished supply of oxygen in the lungs and blood always induces a diminution of the content of carbon dioxide also by overbreathing and in other ways; and that not only does a deficiency of oxygen induce acapnia, but that acapnia in turn tends to intensify the deficiency of oxygen; for it depresses respiration and renders the blood less ready to give up oxygen to the tissues. The relation between anoxia and acapnia is thus the heart of the problem of asphyxia. . . oxygen is an essential food, but not a stimulant. Carbon dioxide, on the contrary, is a tonic and a stimulant: a stimulant that now annually saves thousands of lives."

The author, so your reviewer believes, successfully explodes the theory that asphyxia is essentially a state of acidosis by presenting evidence that carbon-dioxide administration is beneficial in asphyxia and harmful, or even lethal, in true acidosis, such as one induced by the administration of a mineral acid. The terms acidosis and alkalosis, or alkali reserve, moreover, are inherently confusing because without further description of the state named there is great difficulty in knowing what is meant by them. A lowered pH of the blood does not of necessity mean that an acidosis exists that must be combated by alkali. It may be one that can be successfully relieved by acid in the form of carbon dioxide. The pH of the blood is not an inherent quality, it is imposed upon the blood by the volume of the breathing at the moment. Excessive ventilation of the blood in the lungs induces a pH above normal, depressed ventilation a pH below normal. "High and low pH do not indicate alkalosis and acidosis. They indicate only the activity of respiration in comparison with the amount of alkali in use in the blood."

The activity of respiration is determined by the activity of the respiratory center, which controls it. Furthermore, the activity of the center is determined not merely by the stimulus applied to it, but by its own level of excitability. The latter can be altered through a variety of agencies, some of which, notably oxygen want, also pain, fever, alcoholic intoxication and the excitement stage of ether anesthesia, increase excitability, while others, such as sleep, high oxygen and morphine, depress it.

With regard to the amount of alkali in use in the blood, the author claims that, when carbon-dioxide tension in the lungs is increased, alkali is called into the blood from the tissues, and vice versa. This shift between blood and tissue with respect to base under the control of carbon-dioxide tension is an important part of his conception of the physiology of breathing. Oxygen want, he avers, "first alters the excitability of the respiratory center; respiration then by overventilation throws the relation of H_2CO_3:$BHCO_3$ in the blood out of balance; and the tissues, through a shift of alkali, restore the balance."

Following the chapters on the physiology of breathing is a series of chapters on pathologic states and their treatment in which the breathing is importantly concerned. Mountain sickness and acclimatization to high altitude come first, then carbon-monoxide asphyxia. With regard to the latter the author has proved beyond doubt that the liberation of carbon monoxide from the blood and, consequently, recovery from asphyxia are more rapid when the poisoned subject breathes either air or oxygen, preferably the latter, enriched with carbon dioxide than when he breathes oxygen alone. The hyperpnea induced by the carbon dioxide leads to a far more rapid blowing off of carbon monoxide than does the inhalation of oxygen alone, and the high tension of carbon dioxide permits the hemoglobin to combine readily with oxygen and thus aids in the relief of asphyxia.

Through the development of the H. H. Inhalator and its addition, on a wide scale, to the equipment of the rescue crews of city fire and police departments, city gas and electric companies, hospital ambulances and mine rescue crews, adequate resuscitation methods from carbon-monoxide asphyxia have been made available to most persons likely to be afflicted.

Asphyxia neonatorum and resuscitation therefrom next

engages the author's attention. He points out that "much of common belief and practice in regard to manual artificial respiration is unsound or even absurd. Compressing the thorax of an apneic baby in which the lungs are still completely atelectatic cannot draw air into them." Gentle insufflation of air and carbon-dioxide mixture will usually start the infant's breathing very successfully.

Concerning postoperative depression, the author emphasizes the role of diminished tonus of the skeletal muscles, especially those of respiration, induced by anesthetics. This leads to diminution in the size of the chest cavity and promotes atelectasis of the lungs. The best way to combat this tendency is to secure elimination of anesthetics as quickly as possible, and this, in the case of the volatile ones, can be accomplished by letting the patient inhale carbon dioxide in suitable concentration.

The chapter on pneumonia seems, to your reviewer, the least convincing in the book. On the theory that atelectasis, the result of poor bronchial drainage, is an important factor in the development of pneumonia, the author again prescribes carbon-dioxide therapy. It is amusing, to the reviewer, that in the treatment of pneumonia we have had recommended both carbon-dioxide treatment to prevent atelectasis and artificial pneumothorax to produce it. In view of the other methods now at hand for the treatment of pneumonia, it is doubtful if either of the aforementioned has any important place in therapeutics.

So-called shock, in which he believed acapnia plays an important role, was one of the first subjects to engage Professor Henderson's attention, nor have the intervening years obliged him to reverse any of his fundamental concepts. Briefly, he believes the condition chiefly due to impaired venous return to the heart, and this, in turn, to decreased tonus of the body musculature resulting from acapnia or, as he now prefers to call it, acarbia. Furthermore, impaired return flow of blood to the heart leads to asphyxia, just as do failure of the heart itself and hemorrhage.

The final chapter is on muscle tonus and artificial respiration. In this he points out that manual artificial respiration is still the most effective emergency method of resuscitation. He also indicates the relation of muscle tonus to the possibility of resuscitation. The atonic thorax cannot be ventilated by any sort of manual manipulation. But tonus can be restored by the inhalation of carbon-dioxide mixtures because this gas not only acts on the respiratory center, but also, so the author believes, exercises a strong tonic effect on the skeletal muscles, thus promoting the natural excursion of the thorax, as well as the return flow of blood to the heart when shock is a factor.

Whether all the author's theoretical structure will endure is doubtful. But at least it can be said that he has used his fertile imagination in a truly scientific manner and that he has pursued facts with vast energy. His facts, for the most part, we can accept as well substantiated. His interpretations occasionally leave us wondering. Professor Henderson deserves more credit than is sometimes accorded him, not only for contributing directly to the knowledge of his subject, but for stimulating a vast amount of work by others, and last, but not least, for contributing, to humanity, methods which have saved many lives.

The book is thought provoking and instructive. It is worth the while of any physician or surgeon to read it.

Carbon Monoxide Asphyxia. Cecil K. Drinker. 276 pp. London, New York and Toronto: Oxford University Press, 1938. $4.50.

This comprehensive monograph, written by a student of the subject for many years, is a scholarly and thorough presentation of the many aspects of carbon-monoxide hazards. It includes chapters on the physiology and biochemistry of the agent; acute poisoning and the problem of aftereffects; what constitutes harmful exposure; statistics and common sources of hazards; the pathology of the condition; the problem of chronic exposure; the treatment of acute exposures; and finally, chemical methods of detection of carbon monoxide in air and in the body.

The significant literature of the subject is covered and an extensive bibliography is appended.

The importance of carbon-monoxide asphyxia becomes evident when we remember that annually in the United States nearly 4000 persons die from this cause. The majority of these deaths are suicidal, but accidental deaths are common and frequently due to preventable causes. Whenever organic matter is burned without adequate oxidation, carbon monoxide is produced. So that in addition to inhalation of illuminating and natural gases, hazards arise from motor-exhaust gas; coal or charcoal gas, smoke in conflagrations, blast-furnace gas, gas from explosions, and the incomplete burning of illuminating and natural gases due to defective equipment or exhaustion of oxygen.

The author is inclined to discount the last factor, namely the exhaustion of oxygen, but, in the opinion of the reviewer, too many deaths have occurred in small closed rooms in which gas heaters in use were not faulty to leave much doubt that the lack of oxygen was a factor, even though gas flames were extinguished prior to serious consumption of oxygen. The temperature of the rooms and the circumstantial data in such cases make it probable that the deaths were accidental.

Doubt is thrown on the constancy with which the blood remains fluid in carbon-monoxide poisoning, but experience of the reviewer in the examination of bodies, even at long periods after death, is that fluid blood will be found. Thromboses in small vessels, as in the brain, may occur, but they are found in persons who have survived the immediate exposure to the gas and are apparently due to local damage to vessels at the sites of thrombosis, that is, are of secondary production.

The somewhat moot question of chronic carbon-monoxide poisoning is given thorough study. It is accepted that recovery from the immediate effects of exposures which result in prolonged unconsciousness may be followed by serious effects due to brain anoxia. It is agreed that persons with diseased organs, notably heart conditions, are much more prone to succumb to given exposures to carbon monoxide than are normal individuals. It has been demonstrated that acclimatization to carbon monoxide may result from repeated exposures, and may be associated with an increase of red cells to add to the oxygen-carrying capacity of the blood. The indefinite character of some of the subjective symptoms, such as gastrointestinal disturbances, insomnia, depression, irritability, burning of the eyes, ringing in the ears and palpitation, leads the author to be properly critical of the diagnosis of chronic carbon-monoxide poisoning in individuals repeatedly exposed to small amounts of carbon monoxide. That the individuals who complain of these symptoms are frequently neurotics adds to the doubt of a specific relation in many of these cases. Some of the cases which have been reported, however, are recognized as indicating that there is a syndrome associated with long-continued exposure to minor amounts of carbon monoxide which is prone to manifest itself in substandard individuals.

The procedures for resuscitation of subjects of carbon-monoxide exposure are well covered, with illustrations of the various methods of artificial respiration.

The book is a welcome addition to the literature on an important subject and is highly recommended.